Department of Defense
Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **21 NOVEMBER 2002**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee Meeting

1. A meeting of the DoD P&T Committee convened at 0800 hours on 21 November 2002, at the Uniformed Services University of the Health Sciences, Bethesda, Maryland.

2. VOTING MEMBERS PRESENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL Joel Schmidt, MC	Army
MAJ Travis Watson, MS	Army
COL John R. Downs, MC (via VTC)	Air Force
COL Bill Sykora, MC	Air Force
LtCol George Jones, BSC	Air Force
CAPT Matt Nutaitis, MC	Navy
CDR Kevin Cook, MSC	Navy
CAPT Robert Rist	Coast Guard
Kathy Tortorice (Representing Dick Rooney)	Department of Veterans Affairs
Dr. Trevor Rabie	Uniformed Services Family Health Plan

VOTING MEMBERS ABSENT

Physician	Army

OTHERS PRESENT

LTC Marc Caouette, MS	Joint Readiness Clinical Advisory Board
Howard Altschwager	Deputy General Counsel, TMA
CAPT Joe Torkildson, MC, USN	DoD Pharmacoeconomic Center
LtCol Dave Bennett, USAF, BSC (via VTC)	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC, USN	DoD Pharmacoeconomic Center
Maj Barb Roach, USAF, MC (via VTC)	DoD Pharmacoeconomic Center
CDR (sel) Ted Briski, MSC, USN	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
David Bretzke (via VTC)	DoD Pharmacoeconomic Center
Eugene Moore (via VTC)	DoD Pharmacoeconomic Center
Angela Allerman (via VTC)	DoD Pharmacoeconomic Center
LT Chad McKenzie (via VTC)	DoD Pharmacoeconomic Center, Idaho State PharmD Internship
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
MAJ John Howe, MS	Defense Supply Center Philadelphia
Paul Vasquez	Defense Supply Center Philadelphia
Vincent Valinotti	Defense Supply Center Philadelphia
Mark Petruzzi	Medco Health
Elizabeth Scaturro	Medco Health
Victor Diaz, MD, MPH	Humana
William Hudson	Humana
Gene Lakey	TriWest
Ray Nan Berry	Health Net Federal Services
Lisa LeGette	DoD Tricare Information Center
LTC Emery Spaar	U.S. Army Officer resident at AMCP

3. REVIEW MINUTES OF LAST MEETING– The minutes from the last meeting were accepted as written.

4. INTERIM/ ADMINISTRATIVE DECISIONS –

A. *Membership*: Currently the DoD P&T Committee has 13 voting members. All other members are listed as other attendees. COL Remund will send out a copy of the existing charter to all members and recommendations for changes to the charter regarding membership should be sent to the chairs prior to the March meeting. The Council will decide at that time whether changes need to be made to the charter.

B. *Venlafaxine extended release capsules (Effexor XR) Blanket Purchase Agreement (BPA):* At the August 2002 meeting, the Council voted to add venlafaxine extended release 37.5, 75, and 150 mg capsules to the BCF, contingent on the signing of a BPA between Wyeth-Ayerst and DSCP. The BPA was recently signed, so Effexor XR is now on the BCF and facilities are required to include it on their formularies.

5. **UNIFORM FORMULARY (UF) PROPOSED RULE**- Howard Altschwager, TMA Deputy General Counsel, briefed the Committee on the status of the UF proposed rule. The TMA Pharmacy Program Office is currently in the process of formulating responses to comments submitted by the public.

6. **BCF AND NATIONAL MAIL ORDER PHARMACY (NMOP) FORMULARY ISSUES** – The Committee determined the NMOP formulary status, NMOP or retail network formulary restrictions (quantity limits or prior authorization), and Basic Core Formulary (BCF) status for 13 new drugs or formulations (see Appendix A). The PEC also presented brief information on six additional new drugs or formulations not requiring a complete review by the Committee. The Committee agreed that no further review was required (see Appendix B for comments).

7. **NMOP AND RETAIL NETWORK ISSUES**

A. Review of the NMOP and retail network quantity limits for antiemetics – A review of the quantity limits established for oral 5-HT3 receptor agonists, used for the treatment of chemotherapy-induced nausea and vomiting, was initiated based on an inquiry received from a customer service representative at TMA West. A complaint was filed with this individual by a retired beneficiary, who stated that the quantity limit that currently exists was insufficient to meet the clinical needs of his wife, who was receiving treatment for cancer. CAPT Torkildson (PEC) performed the analysis and reported to the Committee.

There currently are three 5-HT3 receptor antagonists available in the U.S. for prophylaxis or treatment of chemotherapy-induced nausea or emesis: ondansetron (Zofran), granisetron (Kytril), and dolasetron (Anzemet). The P&T Committee established the following quantity limits for these products at their August 1999 meeting. These quantity limits apply both to the NMOP and the retail network:

Table 1: Quantity Limits for 5-HT3 Receptor Antagonists

Drug	30-day quantity limit	90-day quantity limit
Ondansetron tablets and orally disintegrating tablets	15	45
Granisetron tablets	8	24
Dolasetron tablets	5	15

In each case the quantity limit was established based on the drug's use for the FDA-approved indication: the prevention or treatment of chemotherapy induced nausea or vomiting. The first step of the analysis was to determine if additional FDA-approved indications had been added for one or more of these drugs that would materially change the number of tablets needed during a 30- or 90-day period. Since the quantity limits were initially established, the FDA has approved both ondansetron and granisetron for use in the prevention or treatment of nausea and vomiting associated with radiation therapy. Additionally, ondansetron and dolasetron were approved for treatment of postoperative nausea and vomiting. While the latter indication requires no modification in the quantity limit, the former could be associated with the use of a substantially greater number of tablets than specified by the current quantity limits. Based on the doses recommended for prevention or treatment of radiation-induced nausea and vomiting,

as many as 80 tablets of ondansetron or 40 tablets of granisetron could be required in a 30-day period, well above the current 30-day quantity limits for both products.

The second step of the analysis involved determining the actual number of tablets dispensed per prescription from each point of service and comparing these figures to the established quantity limits. In FY02, 29,645 oral 5-HT3 tablet prescriptions were filled in the MHS. Of these, 53% were filled at MTFs, 45% at retail network pharmacies, and 2% at the NMOP. Table 1 provides information regarding the number and percentage of prescriptions filled in each venue that exceed the currently established 30-day and 90-day quantity limits. No standard quantity limits exist at the MTFs; these figures are provided solely for comparison. It is notable that 13%-18% of prescriptions in the retail network exceed the established 30-day quantity limits. The representatives from each of the MCSC pharmacy benefit managers indicated that this was done only after a review was performed to ensure clinical appropriateness. A small number of prescriptions filled in the NMOP exceeded the 90-day quantity limit; Maj Bellemin indicated that this occurred only after a similar review process had taken been performed by him.

Table 2: Number (percentage) of Prescriptions Filled in FY 02 that Exceed Current NMOP and Retail Quantity Limits

		Point of Service		
Drug	**Qty Limit**	**MTF**	**Retail**	**NMOP**
Ondansetron 4 mg	> 15	1708 (52.2)	404 (13.2)	N/A
	> 45	427 (13)	63 (2.1)	1 (1.3)
Ondansetron 8 mg	>15	2897 (32.1)	812 (10.2)	N/A
	> 45	647 (7.2)	159 (2.0)	8 (3.1)
Granisetron 1 mg	> 8	468 (14.4)	196 (18.3)	N/A
	> 24	101 (3.1)	43 (4)	2 (4.1)
Dolasetron 50 mg	> 5	1 (100)	1 (5.6)	N/A
	> 15	1 (100)	0 (0)	0 (0)
Dolasetron 100 mg	> 5	37 (19.3)	177 (13.2)	N/A
	> 15	13 (6.8)	37 (2.8)	3 (5.6)

The conclusion reached by the PEC was that the current quantity limits are not sufficient to meet the clinical needs of patients undergoing radiation therapy. However, it does not appear that this creates a significant problem for patients. This is most likely due to two factors: 1) the low number of patients requiring treatment with antiemetics during their radiation therapy. Studies have suggested that only patients receiving higher dose abdominal radiation and some patients receiving radiation therapy to the head and neck will require antiemetic therapy. 2) a fair and effective review process for approval of prescriptions that exceed the established quantity limits. This is supported by the fact that only one complaint has been forwarded to the PEC in the three years since the quantity limits were established. Given the growing number of 5-HT3 receptor antagonist prescriptions being written for off-label indications such as hyperemesis gravidarum, the committee felt it would not be prudent to increase the quantity limits above the current levels, as these prescriptions should all be reviewed for clinical appropriateness. The PEC will monitor the situation and report back if the need arises.

8. **CONTROLLED DISTRIBUTION OF PRESCRIPTION DRUGS** – Gamma hydroxy butyrate solution (Xyrem) has been approved by the FDA with distribution limited to a single pharmacy, Express Scripts' Specialty Distribution Services. Since Express Script's Specialty Distribution Services may not be a member of each MCSC network, patients will likely have to file out-of-network claims to get reimbursed for this drug. The MCSC Pharmacy Directors will look into enrolling Express Scripts into their networks so only a copay will be required.
9. **ADJOURNMENT –** The meeting adjourned at 1130 hours. The next meeting will be held at Fort Sam Houston, TX at 0800 on Thursday, 6 March 2003. All agenda items should be submitted to the co-chairs no later than 14 February 2003.

<signed>
DANIEL D. REMUND
COL, MS, USA
Co-chair

<signed>
TERRANCE EGLAND
CDR, MC, USN
Co-chair

List of Appendices

APPENDIX A: NEWLY APPROVED DRUGS CONSIDERED FOR THE NATIONAL MAIL ORDER PHARMACY FORMULARY AND DOD BASIC CORE FORMULARY

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP and/or retail network formulary restrictions**	**BCF Status**
Amoxicillin clavulanate extended release tablets (Augmentin XR; GSK)	2 Oct 02: Treatment of community acquired pneumonia (CAP) or acute bacterial sinusitis caused by beta-lactamase-producing bacteria or *Strep. pneumoniae* with reduced susceptibility to penicillin (e.g., penicillin MICs = 2 mcg/ml). Not indicated for treating infections due to *S. pneumoniae* with penicillin MIC [≥] 4 mcg/ml, due to only limited data. This formulation has 62.5 mg of clavulanate, instead of 125 mg found in other Augmentin preparations. The dose cannot be duplicated with existing Augmentin preparations. Augmentin XR still requires twice daily dosing; the controlled release mechanism appears to provide higher sustained blood levels of amoxicillin.	Added to the NMOP Formulary	**Quantity Limits** General Rule applies **Prior Authorization:** None	Not added to the BCF The BCF listing for amoxicillin/ clavulanate acid oral was clarified to exclude Augmentin XR **Similar BCF agents:** Amoxicillin/ clavulanate is listed on the BCF. The listing includes the pediatric suspension Augmentin ES-600. A generic version of Augmentin is now available.
Tazarotene 0.1% topical cream (Avage; Allergan)	2-Oct 02: Tazarotene is a retinoid prodrug. As Avage, it is indicated for palliation of facial fine wrinkling, hyper- and hypo-pigmentation, and benign facial lentigines in patients using skin care and sunlight avoidance programs. The same active ingredient (0.1% tazarotene) is marketed in a gel formulation under the trade name Tazorac, with indications for the treatment of psoriasis and acne vulgaris.	The Avage brand of tazarotene was specifically excluded from the NMOP Formulary, since its use is limited to cosmetic applications; other drugs intended solely for cosmetic use as a result of the aging process have been determined to be excluded from coverage by TRICARE rule. Tazorac usage will be monitored for any changes in age distribution.	**Quantity Limits** General rule applies. **Prior Authorization** None	Not added to the BCF. **Similar BCF agents:** Tretinoin 0.05% and 0.025% topical cream is listed on the BCF; the listing excludes Renova, a product that is only indicated for wrinkles.
Clindamycin 1% / benzoyl peroxide 5% topical gel (Duac; Steifel Labs)	26 Aug 02: Topical treatment of inflammatory acne vulgaris. This is the second clindamycin 1% / benzoyl peroxide 5% combination product to become available. The other product (BenzaClin; Aventis) is available in 25 and 50-gram jars that require reconstitution prior to dispensing. The Duac product does not require reconstitution; it is available in a 45-gram tube.	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: Clindamycin 1% solution

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP and/or retail network formulary restrictions**	**BCF Status**
Glipizide / metformin tablets (Metaglip; BMS)	21 Oct 02: Initial therapy in type 2 diabetics who are not achieving adequate glycemic control with diet and exercise alone. Also approved for second-line therapy in patients with type 2 diabetes who are not achieving adequate glycemic control with diet, exercise, and initial treatment with metformin or a sulfonylurea.	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: Metformin is listed on the BCF; a mandatory source contract is in effect. Glipizide immediate release is also listed on the BCF
Rosiglitazone / metformin tablets (Avandamet; GSK)	10 Oct 02: Use as an adjunct to diet and exercise in type 2 diabetics who are already receiving rosiglitazone and metformin as separate tablets, or who are not adequately controlled with metformin alone (second line therapy). Avandamet is not labeled for use as initial therapy in type 2 diabetics.	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents:** Metformin is listed on the BCF; a mandatory source contract is in effect. The DoD P&T committee has recommended addition of a TZD to the BCF; a contracting solicitation is in progress.
Dutasteride tablets (Avodart; GSK)	9 Oct 02: Treatment of symptomatic benign prostatic hyperplasia (BPH) in men with an enlarged prostate to include: Symptom reduction of BPH Reduction of the risk of urinary retention associated with BPH Reduction of the risk of BPH-related surgery	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: None. The alpha-blockers terazosin and prazosin are BCF items
Ethinyl estradiol 25 mcg / norgestimate tablets (Ortho Tri-Cyclen Lo; Ortho McNeil)	22 Aug 02. Prevention of pregnancy. Oral tri-phasic contraceptive containing 25 mcg of ethinyl estradiol, and three different doses of norgestimate, a low androgenic-potential progestin. Ortho Tri-Cyclin Lo is not indicated for acne.	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: No low estrogen triphasic OCPs are listed on the BCF. A low-dose monophasic preparation (20 mcg ethinyl estradiol / 1 mg norethindrone / 75 mg ferrous fumarate (Loestrin FE or its generic equivalent) was added to the BCF at this meeting.

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP and/or retail network formulary restrictions**	**BCF Status**
Alosetron tablets (Lotronex; GSK)	7 Jun 02; treatment of severe diarrhea-predominant irritable bowel syndrome in women who have failed to respond to conventional therapy. Alosetron is not expected to be available until Dec 2002. A controlled distribution program is in place that requires physician self-certification and stickers to be placed on all prescriptions. More information is available on the FDA web site at http://www.fda.gov/cder/drug/infopage/lotronex/lotronex.htm. Alosetron was originally pulled off the market in Jun 2000 due to cases of GI toxicity (ischemic colitis ad constipation resulting in 2 deaths). The new indication is narrower than the original labeling, and the dosage is now 1 mg qd instead of 1 mg bid.	Added to the NMOP Formulary. The controlled distribution program requirements can be met through the NMOP, however faxed prescriptions cannot be accepted.	**Quantity Limits** General rule applies; however, the controlled distribution program will necessitate dispensing in pre-packaged quantities. The NMOP will fill Rxs with the amount of tablets that is as close as possible to the original Rx. **Prior Authorization** None	Not added to the BCF **Similar BCF agents:** None
Tegaserod tablets (Zelnorm; Novartis)	6 Aug 02: short-term treatment of constipation-predominant irritable bowel syndrome.	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: None
Adefovir tablets (Hepsera; Gilead)	20 Sep 02 (priority review): treatment of chronic hepatitis B in adults with evidence of active viral replication and either elevations in ALT or AST, or histologically active disease. Labeling has evidence of efficacy for lamivudine-resistant hepatitis B.	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: None
PEG interferon alfa-2a injection (Pegasys; Roche)	16 Oct 02: treatment of adults with chronic hepatitis C who have compensated liver disease and have not been previously treated with interferon alfa	Added to the NMOP Covered Injectables List	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF. Re-examine potential BCF addition in 3-6 months. **Similar BCF agents:** None
Comments regarding pegylated interferon alfa products for hepatitis C: PEG interferon alfa-2a (Pegasys) is not associated with a patient enrollment program; supplies are expected to be sufficient to meet demand. Schering's peg interferon alfa-2b product (PEG-Intron) previously had a patient enrollment program, but it was recently discontinued. The P&T Committee decided to readdress the potential BCF addition of a pegylated interferon alfa product for hepatitis C in 3-6 months.				

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP and/or retail network formulary restrictions**	**BCF Status**
Ezetimibe tablets (Zetia; Merck)	25 Oct 02: Treatment of: Primary Hypercholesterolemia: Monotherapy – as an adjunct to diet to reduce TC, LDL-C, and Apo B Combination therapy – when administered with a statin as an adjunct to diet to reduce TC, LDL-C, and Apo B Homozygous familial hypercholesterolemia: when used in combination with atorvastatin or simvastatin Homozygous sitosterolemia: as an adjunct to diet	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF. The P&T Committee voted to reconsider BCF addition of ezetimibe in 6 months **Similar BCF agents**: None
Guaifenesin extended release tablets (Mucinex; Adams Labs)	As of 12 Jul 2002, Mucinex (Adams Labs) became the first single ingredient guaifenesin extended release product to be 1) approved as safe and effective under a New Drug Application (NDA) and 2) to be approved as an over-the-counter (OTC) product. As a consequence of approval, the FDA has sent warning letters to manufacturers of guaifenesin extended release products explaining that currently marketed single ingredient guaifenesin extended release products without an approved application are considered misbranded and in violation of section 505(a) of the Food, Drug, and Cosmetic Act (FDCA). In addition, provisions of the Durham-Humphrey amendment (products cannot be marketed as both Rx and OTC products) effectively mean all single ingredient extended release will be OTC products. At least one affected manufacturer is known to be petitioning this action, but it is not known if any single ingredient guaifenesin extended release product other than Mucinex will continue to be available in the near future.	Since single ingredient guaifenesin extended release products are now OTC products, they will no longer be available from the NMOP and will not be included on the NMOP Formulary. Prescription extended release guaifenesin products will be dispensed by the NMOP as long as current supplies permit.	**Quantity Limits** N/A **Prior Authorization** None	The DoD P&T Executive Council removed the BCF listing for guaifenesin 600 mg extended release. MTFs may decide whether to retain the product on their formularies or not. See minutes of the DoD P&T Executive Council meeting for more information.

APPENDIX B: NEWLY APPROVED DRUGS NOT REQUIRING FULL REVIEW BY THE P&T COMMITTEE

Generic (Trade name; manufacturer)	**Indication**	**Comments**
Oxaliplatin injection (Eloxatin; Sanofi)	Treatment of metastatic colon/rectal CA in combination with 5-FU and leucovorin.	Not considered for the NMOP Formulary since the injection is not designed for self-administration. Not considered for the BCF due to the specialized nature of the indication.
Rasburicase injection (Elitek; Sanofi)	Orphan drug for the management of uric acid levels in pediatric patients receiving chemotherapy.	Not considered for the NMOP Formulary since the injection is not designed for self-administration. Not considered for the BCF due to the specialized nature of the indication.
Urokinase injection (Abbokinase; Abbott)	Treatment of thrombolysis of acute PE. Indication for catheter clearance is underway. Re-introduced 10 Oct 02, following market withdrawal in 1999 due to manufacturing problems.	Not considered for the NMOP Formulary since the injection is not designed for self-administration and because of the emergent nature of the indication. Not considered for the BCF due to the specialized nature of the indication and the emergent nature of the indication.
Buprenorphine / naloxone; buprenorphine tablets (Suboxone; Subutex; Schering Plough)	Treatment of opioid dependence. Patients can be treated in MD offices outside of methadone maintenance programs. Controlled distribution program is in effect.	Not considered for the NMOP Formulary because a legal interpretation is needed to determine if treatment of opioid dependence outside of a methadone maintenance program is a covered Tricare benefit. It is not known if requirements of the controlled distribution program could be meet in the NMOP. Not considered for the BCF due to the specialized nature of the indication.
Sodium oxybate (gamma hydroxy butyrate) solution (Xyrem; Orphan Medical)	Treatment of cataplexy related to narcolepsy	Not considered for the NMOP Formulary because availability from the NMOP is not feasible; the restricted distribution program for this product is limited to a single pharmacy (see Paragraph 8 in these minutes). Not considered for the BCF due to the specialized nature of the indication.

APPENDIX C: COMBINED SUMMARY OF FORMULARY CHANGES FROM THE DOD P&T EXECUTIVE COUNCIL MEETING AND THE DOD P&T COMMITTEE MEETING

1. BCF CHANGES

A. Additions to the BCF

1) Tolterodine extended release capsules (Detrol LA)
2) Timolol maleate, solution, gel-forming 0.25%, 0.5% (Timoptic XE; Merck brand only - mandatory source contract)
3) Norethindrone/EE/ferrous fumarate 1/0.02 mg (Loestrin FE or its generic equivalent [Microgestin FE])
4) Niacin extended release tablets (Niaspan)
5) Venlafaxine extended release capsules (Effexor XR)

B. Deletions from the BCF

1) Niacin immediate release oral
2) Guaifenesin 600 mg extended (sustained) release tablets

C. Changes and clarifications to the BCF - None

D. Exclusions from the BCF

1) Paroxetine controlled release (Paxil CR) was excluded from the BCF listing for paroxetine
2) Amoxicillin/clavulanate extended release tablets (Augmentin XR) were excluded from the BCF listing for augmentin/clavulanate acid oral

2. NMOP FORMULARY CHANGES

A. Additions to the NMOP Formulary

1) Augmentin/clavulanate acid extended release tablets (Augmentin XR; GSK)
2) Clindamycin 1%/benzoyl peroxide 5% topical gel (Duac; Steifel Labs)
3) Glipizide / metformin tablets (Metaglip; BMS)
4) Rosiglitazone/metformin tablets (Avandamet; GSK)
5) Dutasteride tablets (Avodart; GSK)
6) Ethinyl estradiol 25 mcg/norgestimate (varying doses) tablets (Ortho Tri-Cyclen Lo; Ortho McNeil)
7) Alosetron tablets (Lotronex; GSK) – The controlled distribution program requirements can be met through the NMOP, however faxed prescriptions cannot be accepted.
8) Tegaserod tablets (Zelnorm; Novartis)
9) Adefovir tablets (Hepsera; Gilead)
10) PEG interferon alfa-2a injection (Pegasys; Roche) – added to the NMOP Covered Injectables List
11) Ezetimibe tablets (Zetia; Merck)

B. Exclusions from the NMOP Formulary

1) Avage brand of tazarotene 0.1% topical cream (Allergan) – specifically excluded from the NMOP Formulary, since its use is limited to cosmetic applications; other drugs intended solely for cosmetic use as a result of the aging process are not available from the NMOP.

C. Removed from the NMOP Formulary; no longer available from the NMOP

1) Single ingredient guaifenesin extended release tablets – approved as an OTC product 12 July 02

D. Clarifications to the NMOP Formulary - None

3. **QUANTITY LIMIT CHANGES (NMOP AND RETAIL NETWORK) -** None

4. **CHANGES TO THE PRIOR AUTHORIZATION PROGRAM (NMOP AND RETAIL NETWORK)** - None

Department of Defense
Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **20 November 2002**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Executive Council Meeting

1. The DoD P&T Executive Council met from 0800 to 1515 hours on 20 November 2002 at the Uniformed Services University of the Health Sciences, Bethesda, Maryland.

2. VOTING MEMBERS PRESENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL Joel Schmidt, MC	Army
MAJ Travis Watson, MS	Army
COL John R. Downs, MC (via VTC)	Air Force
COL Bill Sykora, MC	Air Force
LtCol George Jones, BSC	Air Force
CAPT Matt Nutaitis, MC	Navy
CDR Kevin Cook, MSC	Navy
CAPT Robert Rist	Coast Guard
Kathy Tortorice (Representing Dick Rooney)	Department of Veterans Affairs

VOTING MEMBERS ABSENT

Physician	Army

OTHERS PRESENT

COL Geoffrey W. Rake, MC	Medical Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
CAPT Betsy Nolan, MSC	Navy Pharmacy Specialty Leader
COL Mike Heath	Army Pharmacy Consultant Chair, DoD Pharmacy Board of Directors
MAJ John Howe, BSC	Defense Supply Center Philadelphia
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
Paul Vasquez	Defense Supply Center Philadelphia
Vincent Valinotti	Defense Supply Center Philadelphia
LTC Marc Caouette, MS	Joint Readiness Clinical Advisory Board
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
COL Doreen Lounsbery, MC	DoD Pharmacoeconomic Center
LtCol Dave Bennett, BSC (via VTC)	DoD Pharmacoeconomic Center
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CDR (sel) Ted Briski, MSC	DoD Pharmacoeconomic Center
LtCol Barb Roach, MC (via VTC)	DoD Pharmacoeconomic Center
LT Chad McKenzie, MSC (via VTC)	DoD Pharmacoeconomic Center, Idaho State PharmD Internship
Shana Trice	DoD Pharmacoeconomic Center
Dave Bretzke (via VTC)	DoD Pharmacoeconomic Center
Eugene Moore (via VTC)	DoD Pharmacoeconomic Center
Angela Allerman (via VTC)	DoD Pharmacoeconomic Center
CAPT Sandra Yerkes, MC	Deputy, Chief Medical Corps BUMED
LTC Emery Spaar, MS	U.S. Army Officer resident at AMCP
Michael Valentino	Department of Veterans Affairs, PBM

3. REVIEW MINUTES OF LAST MEETING

The minutes from the last meeting were accepted as written.

4. INTERIM DECISIONS/ADMINISTRATIVE ISSUES

A. *Membership*: Currently the DoD P&T Executive Council has 12 voting members and the DoD P&T Committee has 13 voting members. All other members are listed as others present. COL Remund will send out a copy of the existing charter to all members and recommendations for changes to the charter regarding membership should be sent to the chairs prior to the March meeting. The Council will decide at that time whether changes need to be made to the charter.

B. *Venlafaxine extended release capsules (Effexor XR) blanket purchase agreement (BPA):* At the August 2002 meeting, the Council voted to add venlafaxine extended release 37.5, 75, and 150 mg capsules to the BCF, contingent on the signing of a BPA between Wyeth-Ayerst and Defense Supply Center Philadelphia (DSCP). The BPA was recently signed, so Effexor XR is now on the BCF and facilities are required to include it on their formularies.

5. NATIONAL PHARMACEUTICAL CONTRACTS AND BLANKET PURCHASE AGREEMENTS (BPAs)

Contract awards, renewals, and terminations

- New joint DoD/VA contracts were awarded for albuterol inhaler and lisinopril (West-ward; bottles of 100 effective November 21, 2002 and bottles of 1000 effective March 2003).
- The following joint DoD/VA contracts were not awarded because the bid prices were higher than existing FSS prices: penicillin, amoxicillin, dicloxacillin, and cephalexin.
- The following joint DoD/VA contract is in various stages of solicitation: tretinoin cream.

6. PENDING PROCUREMENT INITIATIVES

A. Status of contracting initiatives

- The joint DoD/VA solicitation for a leutinizing hormone releasing hormone (LHRH) agonist has closed. An award is expected in January 03.
- A joint DoD/VA solicitation will not be issued for a nasal corticosteroid. A DoD/VA incentive agreement for fluticasone (Flonase) is being developed and will likely be finalized in December 02.
- A joint DoD/VA solicitation for a "triptan" has been issued and is scheduled to close in early December.
- A revision of the current incentive agreement for levofloxacin is being negotiated.
- A joint DoD/VA solicitation is being developed for an angiotensin receptor blocker (ARB) and is scheduled to be issued during the first quarter of CY 03.
- A joint DoD/VA solicitation for a "statin" is scheduled to be issued in late December 02.
- A joint DoD/VA solicitation for a thiazolidinedione is being developed. A projected issue date is not yet identified.
- The lisinopril contract has been awarded. Details are available at: http://www.dmmonline.com/pharm/indivdrugs.asp?id=83

B. Proposed BPA for tolterodine extended release capsules (Detrol LA) – In June 2001 the Council discussed the drugs used for treating overactive bladder (OAB) in response to several requests to add Detrol LA to the Basic Core Formulary (BCF). At that time the Council concluded that none of the drugs should be added to the BCF because none of them offered sufficient clinical benefit to justify their significantly higher cost compared to oxybutynin immediate release. Pharmacia is now offering a BPA that would reduce the price of Detrol LA if it were added to the BCF.

The Council considered the following information:

- A head-to-head study of Ditropan XL and Detrol LA found that Detrol LA was better tolerated (patients' perceptions reported on a visual analog scale) and slightly more effective (patients' perceptions reported on a 6-point Likert scale)
- An analysis of PDTS data from Jul 01 to Oct 02 showed that 58.4% of patients prescribed Detrol LA obtained at least one refill of their prescription, compared to only 36.7% for Detrol, 36.1% for Ditropan XL, and 30.7% for oxybutynin immediate release. The higher

refill rate for Detrol LA may indicate that patients tolerate it better than other agents and/or that patients perceive that it works better than the other agents.

- Dr. John Fischer, an Air Force urogynecologist, briefed the Council via VTC on his clinical experiences with patients and patient perceptions of benefit. Dr. Fischer recommended that the Council add Detrol LA to the BCF.
- Detrol LA usage has increased much more than other agents for OAB. Data from all outpatient pharmacy points of service in the MHS show that the number of patients getting prescriptions filled for Detrol LA more than tripled from 4,000 patients in Jul 01 to nearly 13,000 patients in Oct 02.

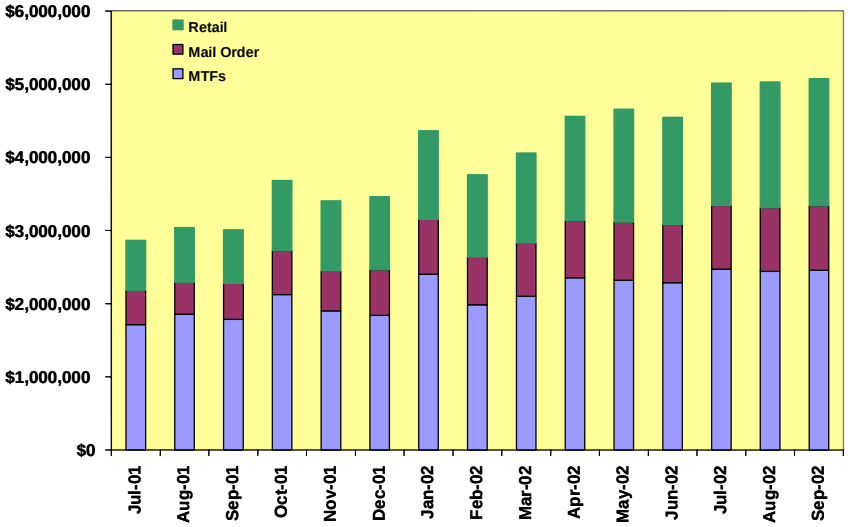
The Council voted to add Detrol LA to the BCF and advise DSCP to accept the proposed BPA.

7. **GENERIC CONTRACTS -** CDR (sel) Ted Briski informed the Council that some solicitations for joint DoD/VA generic contracts do not elicit competitive bids because the generic companies have trouble meeting the large demand from both agencies. He asked the Council whether the need for standardization was still a legitimate reason for pursuing these contracts. Council members stated that standardization is needed by both agencies, particularly to support the use of automation. The Council suggested the two agencies might be more successful by pursuing separate contracts to avoid overwhelming the production capabilities of the generic manufacturers. CDR (sel) Briski stated he would work with the Federal Pharmacy Executive Steering Committee (FPESC) sub-committee for contracting to find viable solutions to the problems encountered. The Council unanimously agreed on the motion to strive to achieve inter-agency standardization through whatever means are available.

8. **ARB Place In Therapy (PIT) Recommendation –** The Council discussed a draft of the Angiotensin II receptor blocker (ARB) place in therapy recommendations. The Council had requested guidelines for ARB use at the last meeting as part of their decision to pursue a procurement strategy to select one of these agents for BCF status, as these agents are significantly more expensive than ACE inhibitors, and their place in therapy is not yet clearly defined. The PIT recommendation is intended to aid practitioners in the appropriate use of the ARBs, and provides a summary of the literature for use in hypertension, congestive heart failure, and diabetic nephropathy. COL Downs expressed concern about the designation of ARBs as the initial agents of choice for diabetic nephropathy in Type 2 diabetes. Members also expressed concern about placement of pricing information at the beginning of the document. The Council asked the Pharmacoeconomic Center (PEC) to work with COL Downs to revise the document and report back at the next meeting.

9. **DRUG CLASS EVALUATIONS TO DETERMINE CLINICALLY ACCEPTABLE CONTRACTING/FORMULARY STRATEGIES**:

   A. Bisphosphonates — Oral bisphosphonates are the most frequently prescribed drug therapy for the treatment of osteoporosis. Alendronate and risedronate are currently indicated for the prevention and treatment of postmenopausal osteoporosis, glucocorticoid-induced osteoporosis, and Paget's disease. Alendronate is also indicated for osteoporosis in men. Both bisphosphonates are available in daily or weekly dosing formulations. The weekly dosage forms account for the majority of DoD usage. The DoD now spends about $5 million a month on oral bisphosphonates across all outpatient pharmacy points of service. Bisphosphonates rank number 8 in Military Treatment Facility (MTF) overall drug expenditures.



MHS Bisphosphonate Monthly Expenditures

Source: PDTS & Prime Vendor Data

Therapeutic Interchangeability:

- *Efficacy* – There are no head-to-head trials that compare fracture rates for alendronate and risedronate. Tables 1-4 in Appendix A show 'funnel' diagrams of the relative risk of vertebral and non-vetebral fractures for each drug compared to placebo from a recently published meta-analysis. Table 5 in Appendix A shows the results of studies that compared each drug to placebo for hip fractures. In their responses to a PEC survey, 50 out of 57 DoD providers stated that they believe alendronate and risedronate have similar efficacy. The Council concluded that alendronate and risedronate have similar efficacy in reducing fractures.
- *Safety/Tolerability* – Oral bisphosphonates are well tolerated when taken according to manufacturers' recommendations. Clinical trials show adverse event rates that are not statistically different from placebo, but gastrointestinal disturbances (sometimes severe) can occur if patients do not follow dosing instructions. Two head-to-head trials examined the tolerability of alendronate and risedronate. The first head-to-head trial compared 28-day regimens of alendronate 40 mg and risedronate 30 mg. The study failed to find a statistically significant difference in endoscopically diagnosed ulceration or patient-reported GI toxicity. The second study evaluated 14-day regimen of alendronate 10 mg and risedronate 5mg. A significant difference in endoscopically diagnosed ulceration was found for gastric ulcers (13.2% for alendronate group and 4.1% for risedronate group), but not for esophageal or duodenal ulcers. No significant difference in patient-reported upper GI adverse events was seen between each group and no correlation was found between upper GI events and the presence or absence of gastric or esophageal ulcers. An accompanying editorial regarding this study stated, "the clinical relevance of small endoscopic ulceration observed is unclear." The editorial also stated, "it is controversial whether acute endoscopically diagnosed superficial mucosal injury (including gastric ulcers as small as 3mm in diameter) is at all related to subsequent development of serious clinical consequences..." The Council concluded that alendronate and risedronate are similar in regard to safety and tolerability.

Coverage of Clinical Needs: Although alendronate is the only bisphosphonate that has an FDA-approved indication to increase bone mass in men with osteoporosis, an analysis of DoD prescription data showed that the percent of total days of therapy dispensed to men were similar for both alendronate and risedronate. The difference in FDA-approved indications does not

appear to affect usage of the two drugs in clinical practice. The Council concluded that either agent would likely meet the clinical needs for more than 90% of the population requiring treatment.

Provider Acceptance:

- *New Starts*- The majority (48 - 7) of providers responding to a PEC survey were willing to use either agent equally. Some providers preferred alendronate because of its indication for osteoporosis in men and perception of greater efficacy in reducing hip fractures.
- *Patient Switches* – The majority (43 - 16) of providers were also willing to switch current patients to the selected agent if the switch could be done at a regularly scheduled visit rather than incurring an extra visit.

The Council voted unanimously to support any contracting/formulary strategy (to include a closed class contract with patient switches) designed to lower the cost of bisphosphonate drug therapy for DoD.

B. Glaucoma Agents — Primary open-angle glaucoma (POAG) is the most common type of glaucoma. POAG leads to progressive visual field loss followed by central field loss, usually but not always in the presence of elevated intraocular pressure (IOP). Lowering IOP remains the primary modality for therapy for POAG and appears to protect against further damage. The therapy for POAG often is characterized by poor compliance since POAG is entirely asymptomatic.

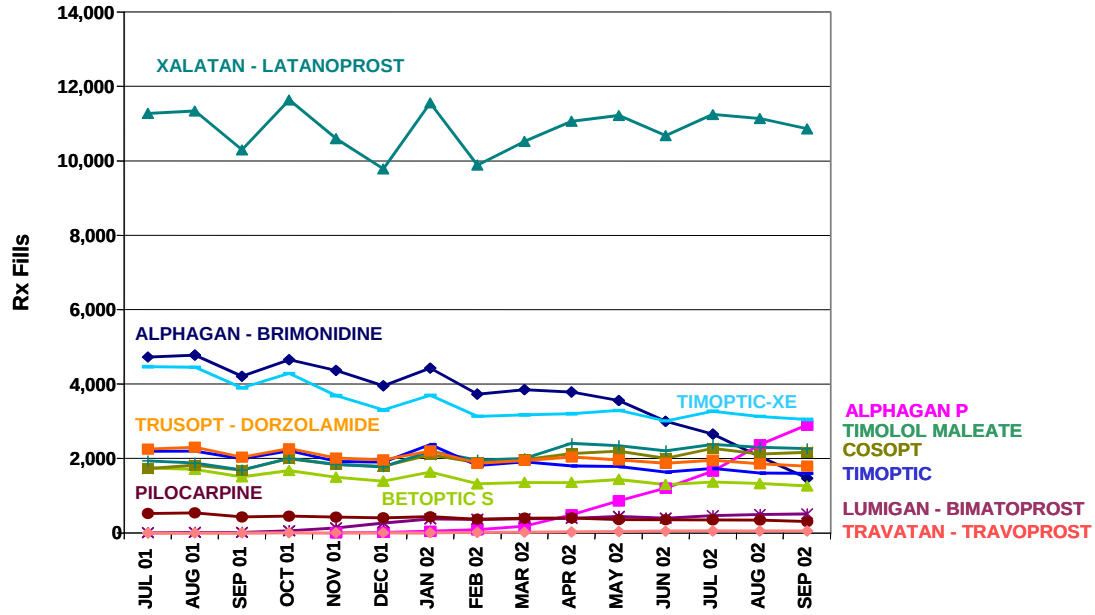
High utilization of latanoprost (Xalatan) and timolol maleate gel (Timoptic XE), which are not currently on the BCF, and new products for the treatment of glaucoma, triggered this class review. The PEC also received a request from the field to delete pilocarpine from the BCF due to low utilization.

Currently the BCF contains the following glaucoma medications:

- *Topical β-blocker* (timolol 0.25%, 0.5% ophth soln – Alcon Labs brand only- DoD mandatory source contract): This drug effectively lowers IOP by 27-35% and is considered initial drug therapy in primary open angle glaucoma (POAG) and ocular hypertension, except in patients with cardiac or pulmonary contraindications. Topical β-blockers have few ocular side effects, however major side effects are similar to those associated with systemic beta-blocker therapy (worsening of heart failure, bradycardia, heart block, and increased airway resistance). The current BCF listing does not include timolol maleate gel (Timoptic XE), which is applied once daily vs. the twice-daily ophthalmic solution.
- *Sympathomimetic agent* (brimonidine 0.15% ophth soln – Alphagan P): Efficacy studies report a decrease in IOP of 20-27%. These agents are indicated for both short-term treatment to prevent intraocular pressure (IOP) spikes after laser trabeculoplasty and for chronic treatment in patients with ocular hypertension or POAG. The Alphagan Purite 0.15% formulation has a 41% lower rate of ocular allergy than brimonidine 0.2% resulting in a reduced rate of discontinuation due to adverse events.
- *Miotic* (pilocarpine ophthalmic solution): Efficacy studies report a decrease in IOP of 20-30%. Pilocarpine's unique place in therapy is in the use for glaucoma emergencies such as acute angle closure glaucoma and glaucoma laser surgery.

MTF RX Fills for Anti-glaucoma Agents

(July 01-September 02)



Source: PDTS

The BCF does not contain medications in the following classes of glaucoma medications:

- *Carbonic anhydrase inhibitors (CAI):* Acetazolamide is the most commonly used oral CAI. These drugs effectively lower IOP by 20-40% with low ocular adverse effects, however their systemic adverse effects hamper their use in the management of glaucoma. These agents are contraindicated in patients with renal failure, hepatic insufficiency, lowered plasma potassium and sodium levels, and chronic obstructive pulmonary disease. Due to low utilization of these agents and their poor tolerability these agents were not considered for BCF inclusion.
- *Prostaglandins (latanoprost, bimatoprost, travoprost, unoprostone)*: These agents are indicated for the reduction of elevated IOP in patients with open angle glaucoma or ocular hypertension who are intolerant of other IOP-lowering medications or insufficiently responsive to another IOP-lowering medication.

Despite their "second line" place in therapy, the prostaglandin class has been targeted for a procurement strategy due to increased utilization, increased cost, and potential for price competition due to the number of agents in the market basket. A significant price reduction might be achieved through a procurement initiative that places one or more prostaglandin on the BCF. The following analysis focuses on prostaglandins.

Prostaglandin Clinical Efficacy: Clinical trials have not demonstrated *a priori* that treating to predefined IOP targets preserves vision. Nor have there been clinical trials demonstrating that more aggressive IOP lowering targets result in preservation of vision. Limited observational data suggests that patients achieving lower IOP with combined surgical and medical treatment experience less visual field deterioration. Finally, there are no clinical trials comparing the amount of preservation of visual acuity afforded by the different topical ophthalmic drops. All

comparisons of efficacy rely on the surrogate marker of lowering IOP. A measurement error of 1-2 mmHg may be seen in IOP measurement.

Randomized controlled clinical trials demonstrated that bimatoprost, travoprost, and latanoprost given once daily produced equal or superior efficacy to twice-daily timolol. Appendix B shows the results of prostaglandin head-to-head comparison trials.

Prostaglandin Safety and Tolerability: Both bimatoprost and travoprost have shown to have statistically significant more cases of hyperemia and pruritis than latanoprost. Mean hyperemia scores in all treatment groups, however, were in the trace to mild hyperemia range. Local adverse effects seem to be unassociated with long-term effects or increased discontinuation of medications in the clinical trials. See table 1 for adverse events related to prostaglandin ophthalmic agents found in head-to-head comparison trials.

Table 1: Adverse events related to prostaglandin ophthalmics

Study	Adverse Event	Timolol 0.5%	Latanoprost 0.005%	Bimatoprost 0.03%	Travoprost 0.004%	Unoprostone 0.12%
Tin Aung 2001	Ocular irritation	N/A	12/37 (32%)	N/A	N/A	21/34 (62%)
	Iris pigment changes	N/A	0	N/A	N/A	0
	Eye redness	N/A	13/37 (35%)	N/A	N/A	6/34 (18%)
Netland 2001	Hyperemia*	14%	27.6%	N/A	49.5%	N/A
	Iris pigment changes*	0%	5.2%	N/A	3.1%	N/A
	Eyelash changes*	3.1%	25.8%	N/A	57.1%	N/A
Gandolfi 2001	Hyperemia*	N/A	14.2%	36.1%	N/A	N/A
	Iris pigment changes	N/A	Not reported	Not reported	N/A	N/A
	Eyelash changes*	N/A	4.4%	12.6%	N/A	N/A
DuBiner 2001	Hyperemia	N/A	3/21 (14%)	3/21 (14%)	N/A	N/A
	Iris pigment changes	N/A	Not reported	Not reported	N/A	N/A
	Eyelash changes	N/A	Not reported	Not reported	N/A	N/A

Tin Aung: One patient on latanoprost did not complete the study because of severe swelling of the eyelids.
Netland: No reported discontinuations in article due to adverse events
Gandolfi: Six bimatoprost patients discontinued due to adverse events: 4 due to ocular events, 2 due to systemic and ocular adverse events. Five latanoprost patients discontinued due to adverse events: 2 due to ocular events, 3 due to systemic and ocular adverse events.
DuBiner: One patient discontinued from the latanoprost group because of body aches and stomach cramps. Two patients discontinued from the bimatoprost group because of ocular symptoms (eyelid edema, conjunctival hyperemia, foreign body sensation) or nausea and ocular symptoms (eyelid edema, asthenopia, conjunctival hyperemia).

Therapeutic Interchangeability: Unoprostone is not considered therapeutically equivalent to latanoprost, bimatoprost or travoprost because of its lower efficacy (Appendix B, Table 1) and twice-daily dosage schedule. Latanoprost, bimatoprost, and travoprost have each been demonstrated to provide statistically significantly greater reductions in IOP than timolol. Head-to-head trials did not show statistically significant differences between latanoprost and travoprost 0.004% or between latanoprost and bimatoprost in lowering IOP. Post-hoc subgroup analysis of the data from the clinical trial by Netland et al. showed that travoprost lowered IOP more than latanoprost at specific time points among African American study subjects. However, the IOP differences in the travoprost vs. latanoprost group in African American patients during treatment may have resulted from preexisting differences in baseline IOPs, some of which were statistically significant. If the results were expressed as a change in IOP from baseline measurements, no significant difference in efficacy of the drugs in African American population exists. The effect of travoprost in the African American population requires further analysis and clarification.

Both bimatoprost and travoprost may have more hyperemia and pruritis than latanoprost, but less iris or eyelash pigment changes. Mean hyperemia scores in all treatment groups were in the trace and mild hyperemia score. Local adverse effects seem to be unassociated with long-term effects or increased discontinuation of medication in the clinical trials.

Latanoprost currently requires refrigeration prior to dispensing to maintain a 36-month shelf life, while bimatoprost and travoprost do not. The manufacturer of latanoprost has stated their belief that the FDA will eliminate this requirement in early 2003.

Coverage of Clinical Needs: Latanoprost has 95% of the market share in MTFs and 79% in the MHS (MTF, NMOP, and retail). To date there are no studies to show that if one patient fails to respond to one prostaglandin that they will respond to another.

Provider Acceptance: Responses from ophthalmologists agreed that a prostaglandin should be on the BCF. Currently 75% of MTF formularies contain latanoprost, 9% bimatoprost, 4% travoprost, and 2% unoprostone. Providers stated that they are standard second line therapy in the treatment of glaucoma and first line therapy when beta-blockers are contraindicated. Two of the five ophthalmologists preferred latanoprost to other prostaglandins; the other three had no preference. Latanoprost has been on the market longer than the other prostaglandins, so providers have more confidence in its safety profile. Providers were uniformly opposed to a contract that would require patients to be switched from one prostaglandin to another.

Although pilocarpine has low utilization in the MTFs the Council unanimously voted to maintain its BCF status due to its unique place in therapy in the treatment of acute closed angle glaucoma. Timoptic XE has a utilization rate that is consistently higher than the contracted timolol ophthalmic solution, once daily vs. twice daily dosing that may potentially increase compliance, and a current contract price that makes its cost comparable to the ophthalmic solution. The Council unanimously voted to add Timoptic XE to the BCF. The Council voted unanimously to add a prostaglandin to the BCF utilizing a closed class contracting strategy competing latanoprost, bimatoprost and travoprost, which would not require patients to be switched from one agent to another.

10. DRUG/DRUG CLASS EVALUATIONS TO DETERMINE BCF ADDITION

A. *Atypical antipsychotics* –In November 2001, the DoD P&T Executive Council removed oral haloperidol from the BCF due to decreasing utilization and the perception that primary care providers in the outpatient setting do not commonly prescribe antipsychotics. The BCF does not currently include any agents approved specifically for the treatment of psychosis.

After considering the following, the Council agreed that one or more atypical antipsychotic agents are needed on the BCF:

- The PEC received two requests from MTF providers to add one or more atypical antipsychotics to the BCF (one for olanzapine and one for olanzapine and risperidone). The requestors argued that: atypicals are first-line agents in treating psychotic manifestations of psychiatric disorders, they are utilized by civilian and military psychiatrists and should be readily available for continuation treatment, and that typical antipsychotics are no longer standard of care for patients who need long-term therapy.
- All eleven MTF providers (10 psychiatrists, 1 internist) who responded to a PEC survey responded “yes” to the following question: “In your opinion, is there a need to make one or more atypical antipsychotic uniformly available across the MHS by adding it or them to the BCF (which would require all MTFs to add them to their formularies)?”

- Utilization of atypical antipsychotics at MTFs is increasing, both in absolute number of prescriptions and relative to prescriptions for typical antipsychotics.
- An analysis of formulary information from 102 MTFs revealed that 69 facilities had at least one atypical antipsychotic on formulary.
- Atypical antipsychotics are termed atypical due to a decreased propensity to induce extrapyramidal side effects (EPS) and decreased risk of tardive dyskinesia relative to typical antipsychotics. Atypical antipsychotics may also be more effective than typical antipsychotics for treating the negative symptoms of schizophrenia and may be effective in patients refractory to typical antipsychotics.
- Atypical antipsychotics are used for multiple conditions besides schizophrenia (e.g., bipolar mania, depression with psychosis, acute agitation in the elderly; symptoms of dementia including agitation, hyperactivity, hallucinations, suspiciousness, hostility and uncooperativeness; bipolar disorder, anxiety disorders, developmental disorders, autism, aggression/self injurious behavior, and Tourette's syndrome), some of which may be treated by primary care providers. In addition, primary care providers may continue medications written by specialists.
- Addition of an atypical antipsychotic to the BCF may foster the recapture of prescriptions from the retail point of service. However, the potential for recapture may be somewhat limited by the fact that civilian providers write about 50% of prescriptions for atypical antipsychotics filled by MTFs. Overall, civilian providers write about 40% of the prescriptions filled by MTFs (based on prescription data from the Uniformed Services Prescription Database).

The Council unanimously approved a recommendation that the PEC complete its review of the atypical antipsychotics and make a specific recommendation to the Council at the next meeting regarding the number of agents that should be added, and which agent(s) represent the most cost-effective choice.

B. Oral contraceptives – The BCF does not currently include an oral contraceptive (OC) with low estrogen content (20 mcg ethinyl estradiol [EE]). OCs with low estrogen content have a lower risk of venous thromboembolism and other adverse events. The two monophasic OCs with 20 mcg ethinyl estradiol most commonly used in MTFs are norethindrone/EE/ferrous fumarate 1/0.02 mg and levonorgestrel/EE 0.1/0.02 mg. The brand of norethindrone/EE/ferrous fumarate 1/0.02 mg most commonly used in MTFs is Loestrin FE, which is available at a cost of about $0.21 per cycle. A generic equivalent for Loestrin FE, Microgestin FE, is available but is not currently listed on the FSS. The brand of levonorgestrel/EE 0.1/0.02 mg most commonly used in MTFs is Alesse, which is available at a cost of about $6.03 per cycle. A generic equivalent for Alesse, Aviane, is available but is not currently listed on the FSS. Aviane is the most commonly used product in this category in the retail network and NMOP.

After noting that previous attempts to contract for OCs met with limited success, the Council voted to add norethindrone/EE/ferrous fumarate 1/0.02 mg (Loestrin FE or its generic equivalent) to the BCF.

The Council was also informed that a generic version of ethinyl estradiol 35/norethindrone 0.5/0.75/1 mg oral (Ortho-Novum 7/7/7) is expected to be available early in 2003. The Council has previously discussed the difficulty of obtaining the best price for this product, since lower priced "clinic" packs are available only by direct purchase from the manufacturer, not from Prime Vendor, and the previous depot contract expired at the end of February 2002.

C. *Paroxetine controlled release (Paxil CR)* – Paxil CR is a controlled release formulation of paroxetine that shifts absorption to the small intestine and controls release of paroxetine over 4-5 hours. Because of reduced bioavailability, Paxil CR is formulated as 12.5, 25, and 37.5 mg tablets, which are equivalent to 10, 20, and 30 mg of immediate release paroxetine, respectively. Paxil CR was added to the NMOP formulary in May 2002, but it was not added to the BCF because the information available at that time did not demonstrate that Paxil CR offered any significant advantages compared to Paxil. Paxil CR was to be reviewed again at the November 2002 meeting for potential addition to the BCF.

The clinical trials of Paxil CR for major depressive disorder (MDD) included Paxil treatment arms, but the studies were not designed to compare the efficacy of Paxil CR to the efficacy of Paxil. The clinical trials of Paxil CR for treatment of panic disorder did not include Paxil treatment arms.

Pooled data from MDD trials showed that 23% of Paxil patients and 14% of Paxil CR patients reported nausea during the first week of therapy (a statistically significant difference). Statistically significant differences were not seen in the percentages of patients reporting nausea during weeks 2, 3, 4,or 12 of the trials. According to manufacturer information, the dropout rate in the two adult MDD trials was 6% for placebo, 10% for Paxil CR (non-significant difference), 16% for Paxil (significantly higher than placebo). Paxil CR and Paxil were not directly compared. The percentage of patients dropping out due to nausea was 3.7% in the Paxil CR arm and 0.5% in the placebo arm, but patient dropouts due to nausea were not reported for the Paxil arm.

Provider opinion survey results (12 total; 9 from psychiatry) are summarized as follows:

- 1 “add”
- 6 “don’t add”
- 3 “not sure/no opinion”
- 1 “if replaces Paxil at less cost
- 1 “may be some value; slower release may decrease dizziness, vertigo side effects”

Usage of Paxil CR is increasing in the retail network and NMOP, but very few prescriptions for Paxil CR are filled at MTFs. The FSS prices for Paxil CR and all strengths of paroxetine immediate release except the 40 mg tablet are currently the same: $1.31 per tablet ($1.49 for 40 mg). The prices for Paxil and Paxil CR are similar to FSS prices for other SSRIs, with the exception of the $0.04 contract price for generic fluoxetine 20 mg. It is unclear when a generic version of paroxetine will become available; patent litigation has been in progress since 1998.

The Council concluded that Paxil CR has not been shown to offer any significant clinical advantages over Paxil or other SSRIs on the BCF. The four SSRIs currently on the BCF are more than adequate to meet the clinical needs of DoD beneficiaries. The Council also noted that Paxil CR offers no economic advantage over Paxil or other SSRIs on the BCF and that generic fluoxetine is much less expensive than Paxil CR. Inexpensive generic paroxetine will eventually become available. The addition of Paxil CR to the BCF would likely result in higher costs in the long run, because Paxil CR users would be less likely than Paxil users to switch to generic paroxetine when it becomes available. The Council voted unanimously to exclude Paxil CR from the BCF listing for paroxetine. MTFs are not required to add Paxil CR to their formularies.

D. Escitalopram (Lexapro; Forest Labs) – Escitalopram is the S-isomer of citalopram (Celexa; Forest Labs). Citalopram is a racemic mixture (equal amounts of S- and R-citalopram). The s-isomer of citalopram appears to be solely responsible for the antidepressant properties of citalopram. The r-isomer exhibits little binding to serotonin receptors and demonstrates no antidepressant properties. Whether or not the r-isomer results in any clinically significant effect is unclear. Comparable efficacy of 10 mg escitalopram and 40 mg citalopram in clinical trials has led to the theory that the r-isomer may impede binding of the s-isomer at the serotonin receptor or impede receptor function in some other way. The r-isomer does demonstrate affinity for histamine receptors, which could theoretically increase side effects (e.g., sedation) with the racemic mixture compared to the s-isomer alone.

The Committee reviewed escitalopram for addition to the NMOP Formulary in May 2002, just prior to FDA approval. Review of escitalopram for the BCF was tabled until after the drug had been approved by the FDA and was on the market. There are currently four SSRIs on the BCF: citalopram (Celexa); generic fluoxetine - excludes Prozac, Sarafem & Prozac Weekly; paroxetine (Paxil); and sertraline (Zoloft). Forest Labs, which manufactures both citalopram and escitalopram, has ceased promoting citalopram (Celexa), although it will continue to be available. Forest has stated that it does not advocate switching patients who are stable on citalopram or other antidepressants to escitalopram.

Escitalopram is indicated for the treatment of major depressive disorder. The manufacturer's dossier of clinical information for escitalopram includes summaries of the following studies of escitalopram in the treatment of depression:

- Two published 8-week, fixed dose trials, one comparing escitalopram 10 mg to placebo and the other comparing escitalopram 10 mg, escitalopram 20 mg, or citalopram 40 mg to placebo.
- Unpublished data from two 8-week flexible-dose trials comparing escitalopram and citalopram to placebo.
- Unpublished data from a long-term (36 week) extension study
- A published analysis of pooled trial data focusing on anxiety symptoms in depressed patients

Unpublished data addressing the use of escitalopram in generalized anxiety disorder, social anxiety disorder, and panic disorder are also available.

The following table summarizes published efficacy data for escitalopram:

Reference	Trial Design	Primary Endpoint	Results
Burke et al. (J Clin Psych 2002; 63:331-6)	Double-blind, RCT in outpatients aged 18-65 years, with MDD for at least 4 weeks 1-week washout, period, then randomized to 8-week treatment with E10 (n=118), E20 (n=123), C40 (n=125), or placebo (n=119)	Change from baseline in MADRS score at Week 8	Placebo: -9.4 E10: -12.8* E20: -13.9* C40: -12.0*
Wade et al (Int Clin Psycopharmacol 2002; 17(3):95-102)	Double-blind, RCT in primary care patients aged 18-65 years, with MDD for at least 4 weeks 1-week washout period, then randomized to 8-week treatment with E10 (n=191) or placebo (n=189)	Change from baseline to final assessment of MADRS score	Placebo: -13.6 E10: -16.3*
Gorman et al (CNS Spectrums 2002: 7 (suppl 1):40-4)	Pooled data from fixed dose study (E10, E20, C40, placebo) & two flexible dose studies (E10-20, C20-40, placebo) combined n = 1321	Mean change in MADRS score at Week 8	Placebo: -11.2 E: -13.8* C: -13.1*

*p<0.05 vs. placebo
RCT = randomized controlled trial; MDD = major depressive disorder; MADRS = Montgomery Asberg Depression Rating Scale ;E10 = escitalopram 10 mg daily; E20 = escitalopram 20 mg daily; C40 = citalopram 20 mg daily

In the pooled data analysis, two different assessments were evaluated, with two additional analyses of one measure: the Montgomery Asberg Depression Rating Scale (MADRS), the MADRS among patients severely depressed at baseline, the MADRS Inner Tension Item Score, & CGI-I. In each case, the mean change from baseline was determined. For each measure, the mean change from baseline appeared to be significantly different than placebo at earlier time points for escitalopram than for citalopram. Given limited data and the *post priori* nature of the analysis, the existence of a real difference between escitalopram and citalopram with respect to onset of therapeutic effect remains unclear, as do the effect size and clinical importance of any such difference.

Escitalopram appears to have the same generally favorable drug interaction profile as citalopram. Based on available clinical trial data, there is little evidence of differences between the two products with respect to side effect profile. In an 8-week, fixed dose trial (Burke et al) comparing placebo, escitalopram 10 mg, escitalopram 20 mg, and citalopram 40 mg, withdrawal rates due to adverse events were 2.5%, 4.2%, 10.4%*, and 8.8%*, respectively (*p<0.05 vs. placebo). Somnolence occurred in less than 10% of patients in either group.

Provider opinion survey results (12 total; 8 from psychiatry):

- 2 “add”
- 7 “don’t add”
- 1 “too early to tell”
- 1 “add if it’s cheaper”
- 1 “don’t know”

Usage of escitalopram is increasing in the retail network, but very few prescriptions are filled at MTFs or in the NMOP. Forest has offered BPA prices for citalopram and escitalopram. Approval of a generic version of citalopram is not likely until 2005; citalopram’s new molecular entity patent expires July 2003 with a pediatric extension until January 2004.

The Council concluded that escitalopram does not offer significant clinical advantages over citalopram or other SSRIs on the BCF. The four SSRIs currently on the BCF are more than adequate to meet the clinical needs of DoD beneficiaries. The Council also noted that escitalopram offers no economic advantage over citalopram or other SSRIs on the BCF and that generic fluoxetine is much less expensive than escitalopram. Inexpensive generic citalopram will eventually become available. The addition of escitalopram to the BCF would likely result in higher costs in the long run, because escitalopram users would be less likely to switch to generic citalopram when it becomes available. The Council voted unanimously to exclude escitalopram from the BCF. MTFs are not required to add escitalopram to their formularies.

E. Methylphenidate extended release capsules (Metadate CD) – The Council reviewed Metadate CD for inclusion on the BCF, secondary to new clinical information and a BPA offer from Celltech Pharmaceuticals in exchange for placement on the BCF. The Council voted not to add Metadate CD to the BCF. The reasons for this decision were:

- The new clinical information presented by Celltech did not demonstrate that Metadate CD was clinically superior to Concerta.
  - The information provided was a summary of unpublished data that was not peer-reviewed.
  - There were concerns about the study design, statistical methods, and reporting of the results.
  - The assessment tools used to demonstrate the statistical superiority of Metadate CD are not routinely used in clinical practice, making it difficult to determine the clinical relevance of the research findings.
  - These assessment tools appeared to show that the active comparator Concerta was more efficacious at 12 hours post dose.
- Concerta was added to the BCF to take advantage of its long duration of action, which hopefully would eliminate the need for additional immediate release (IR) methylphenidate later in the school day. A subsequent analysis of PDTS data revealed that 7% of patients receiving Concerta required additional doses of IR methylphenidate later in the school day, compared to 43% receiving Ritalin SR. The data provided to the Council suggested that Metadate CD has a shorter duration of action than Concerta; some members of the Council were therefore concerned that it would be less effective than Concerta in eliminating the need for additional doses of IR methylphenidate later in the day.
- MTF providers responded negatively to the proposal to add Metadate CD to the BCF.
- The offered prices in the BPA proposal would not provide a substantial cost avoidance. While the daily cost of therapy would be lower for Metadate CD at low doses of medication, Metadate CD would actually still be more expensive at higher doses. Also, this price consideration does not take into account the increased likelihood of having to add afternoon or evening doses of immediate release methylphenidate to the regimen. The Council also felt it would be extremely unlikely that Metadate CD would achieve a 35% market share given that most providers surveyed were very pleased with the once-daily stimulant currently on the BCF (Concerta).

F. Niacin extended release tablets (Niaspan) – Since the publication of the National Cholesterol Education Program's Adult Treatment Panel III (ATP-III) last year, increasing focus is placed on positively affecting the entire lipid profile by using statin adjuncts for patients with mixed dyslipidemias. The DoD P&T Executive Council evaluated Niaspan (prescription only, extended–release niacin tablets) shortly after its FDA approval. The result was not to add Niaspan to the BCF at that time because sufficient data did not exist to justify its benefit over niacin immediate release therapy. Niacin immediate release oral (OTC) is currently on the BCF.

Since Niaspan's approval, clinical trials using Niaspan in combination with simvastatin and in type 2 diabetics have been published reinforcing niacin's beneficial effects in these populations. The PEC completed a database analysis assessing the tolerability of Niaspan and immediate release niacin treated patients. Niacin-naïve patients beginning Niaspan or other niacins in January and February of 2002 were identified and included for analysis. Patients remaining on therapy at least 6 months later were deemed a success for this analysis. In the Niaspan group, 55% (1676/3044) of the Niaspan group were successful versus 37% (282/769) of the other niacin group were successful in tolerating niacin therapy using continued therapy as the marker.

Niaspan is currently on approximately 40% of MTF formularies and is also on the VA National Formulary. The drug cost for Niaspan remains significantly more than immediate release niacin (~$0.30/tab of Niaspan vs. $0.02/tab of immediate release niacin). Fibrates are the mostly likely alternative to niacin therapy, and the drug costs are comparable ($0.20-$0.85/day) to Niaspan. Fibrates are better tolerated than niacin, but niacin is more effective at raising HDL and is generally considered less likely to cause myopathy than fibrates. Responses from healthcare providers at MTFs were overwhelmingly in favor of adding Niaspan to the BCF.

The Council concluded that niacin therapy remains a recommended treatment in many dyslipidemias. Niaspan significantly improves patient's ability to remain on niacin compared to older formulations, thus reducing the number of patients requiring less effective, and possibly less safe, alternatives.

The Council unanimously voted to replace immediate-release niacin with Niaspan on the BCF. MTFs may continue to have other niacin products on their formularies.

11. DRUG/DRUG CLASS EVALUATIONS TO DETERMINE BCF DELETION

A. Guaifenesin extended release tablets – Based on the following information, the Council voted to remove guaifenesin 600 mg extended release from the BCF. MTFs may decide whether or not to remove the product from their formularies.

- As of 12 July 2002, Mucinex (Adams Labs) became the first single ingredient guaifenesin extended release product to be 1) approved as safe and effective under a New Drug Application (NDA) and 2) to be approved as an over-the-counter (OTC) product.
- The FDA has determined that single ingredient guaifenesin extended release drug products are new drugs and require an approved application for marketing. The Durham-Humphrey Amendment of 1951 to the Food, Drug, and Cosmetic Act (FDCA) forbids simultaneous marketing of products of the same strength, dose, and indication for both OTC and prescription use. Manufacturers can no longer market single ingredient guaifenesin extended release products as prescription drugs. In October 2002, the FDA sent warning letters to manufacturers and distributors explaining that currently marketed single ingredient guaifenesin extended release products without an approved application are considered

misbranded and in violation of section 505(a) of the FDCA. The FDA requested action plans to bring their products into legal compliance. At least one affected manufacturer is known to be petitioning this action, but it is not known if any single ingredient guaifenesin extended release product other than Mucinex will continue to be available in the near future.

- The Council reviewed the issue of OTC coverage on the BCF at the May 2002 meeting. Although TRICARE policy (which limits coverage of OTCs to insulin, diabetic supplies, and vitamins when used as a specific treatment of a medical condition) does not govern the availability of OTC products at MTF pharmacies, the Council has historically refrained from adding OTC products to the BCF. In addition, the Uniform Formulary Proposed Rule states, "The Basic Core Formulary (BCF) is a subset of the Uniform Formulary and is a mandatory component of all MTF pharmacy formularies." If the BCF is to be a subset of the Uniform Formulary, the inclusion of OTCs on the BCF will be limited by TRICARE policy. The Council voted not to add any additional OTC products to the BCF beyond those identified in the TRICARE Policy Manual. The Council encouraged MTFs to continue providing OTC medications when they represent cost-effective alternatives to legend drugs.

As an OTC product, Mucinex will not be available from the retail network or NMOP.

12. MTF REQUESTS FOR BCF CHANGES

A. Requests to add zonisamide (Zonegran) to the BCF – A MTF provider requested the addition of zonisamide to the BCF. The rationale for the request was that zonisamide is a useful and safe drug to use for diabetic peripheral neuropathy, chronic headache syndromes, restless leg syndrome, and chronic back pain. No supporting literature was presented along with the request. CAPT Torkildson performed the analysis and presented the findings to the Council for consideration.

The FDA approved zonisamide in March 2000 as "adjunctive therapy in the treatment of partial seizures in adults with epilepsy". This approval was based on three registration trials that demonstrated statistical and clinical superiority over placebo in treating patients with partial seizures who were inadequately controlled on at least one other antiepileptic drug (AED). There are no data at present supporting its use as monotherapy for partial seizures. Also, despite the statement in the BCF request that zonisamide was useful for the off label indications listed, there are no published data supporting its utility in treating any of the listed conditions. One open-label study was identified that suggested that zonisamide might be of some benefit in treating patients with Parkinson's disease, but this had not yet been confirmed.

Analysis of available safety data raised some concerns. Zonisamide is a sulfonamide derivative, and is contraindicated in patients with an allergy to sulfonamides. Three cases of severe hematologic adverse events (2 cases of aplastic anemia, 1 case of agranulocytosis) have been reported in Japan, where the drug has been on the market for approximately 10 years. Based on the number of patient-years of exposure, the frequency of this adverse event is higher than that observed in the general population. Several cases of oligohydrosis and hyperthermia have been reported in pediatric patients treated with this agent; the FDA added a bolded warning to the package insert in June 2002 notifying prescribers of this concern. Additionally, 4% of 991 patients treated with the drug during its development phase developed renal stones, and in several studies it was noted that patients treated with zonisamide had a mean increase in their BUN and creatinine of 8%, compared to essentially no change in the placebo group. Of particular concern was the fact that these values did not return to baseline following discontinuation of the drug.

Regarding tolerability, it was noted that in several controlled trials the discontinuation rate due to adverse events in the zonisamide group was twice that of the placebo group (12% vs. 6%), while a separate analysis of several trials with a total of 1,336 treated patients revealed that 21% of patients discontinued therapy due to adverse events.

Finally, a utilization analysis revealed that only 61 MTFs filled prescriptions for zonisamide in FY02, only 23 MTFs filled more than 6 zonisamide prescriptions in that year, while 26 sites filled 3 or fewer. During that same period a total of 3,800 prescriptions for zonisamide were filled in the retail network.

Based on this review, the PEC concluded that there was insufficient evidence to support the use of zonisamide for the conditions outlined in the BCF request. Additionally, the level of concern regarding safety is higher for zonisamide than for other products, such as gabapentin, used for the treatment of these conditions. Gabapentin was added to the BCF in August 2002, providing uniform availability of a similar product with a more acceptable safety and efficacy profile. Finally, the overall utilization of this product across the MHS appears insufficient to require all facilities to make this product available. The PEC recommended that zonisamide not be added to the BCF. The Council unanimously approved this recommendation.

B. *Request to add pimecrolimus (Elidel) to the BCF–* A MTF provider requested that pimecrolimus, a topical immunomodulator (TIM), be added to the BCF. This is a new class of topical, nonsteroidal medications indicated for the treatment of atopic dermatitis (AD). Tacrolimus (Protopic) has been available since December 2000, and is FDA approved for treatment of moderate to severe atopic dermatitis. Pimecrolimus (Elidel) has been available since early 2002, and is FDA approved for the treatment of mild to moderate atopic dermatitis. Atopic dermatitis starts in early childhood and causes significant quality of life issues related to the pruritis and appearance of the rash. Ninety percent of AD patients have mild to moderate severity of disease and the rest are moderate to severe.

Efficacy: Randomized-controlled trials demonstrate that both agents are more efficacious than placebo in the treatment of AD. Tacrolimus appears to be as efficacious as a medium potency topical corticosteroid, where pimecrolimus is as efficacious as a low potency topical corticosteroid.

Safety/tolerability: Neither drug has clinically significant adverse effects, which cause the patients to discontinue use. The drugs are not systemically absorbed, so can be used long term without the worries associated with long-term topical corticosteroids (CS) use. They can also be used in sensitive body areas such as the face and intertriginous regions where one would not want to use topical CS.

Other: Provider response was markedly positive regarding the potential of having an alternative to topical steroids for patients that require one. At the same time, providers noted that these will not take the place of the low potency topical CS and the usual initial therapies for mild AD. Pimecrolimus prescription fills in all points of service (MTF, NMOP, and retail) are increasing, with the majority of its use in the very young (ages 0 - 4) and elderly (ages 65+) population. Providers feel that usage will continue to increase significantly in this class.

The Council agreed that topical immunomodulators (TIMS) are a unique class and have a substantial place in therapy for the treatment of AD, however there is concern regarding the cost of these agents and the potential for misuse. The Council agreed to consider one or both of these medications for addition to the BCF at their next meeting. They asked the PEC to explore procurement options and report back in three months.

13. DEPLOYMENT FORMULARY AND SUPPORTING HOMELAND SECURITY (JRCAB) – LTC Marc Caouette presented information and a short brief on homeland security and deployment formulary to the DoD P&T Executive Council.

14. ADJOURNMENT

The meeting adjourned at 1530 hours on 20 November 2002. The next meeting will be held at Fort Sam Houston, TX at 0800 on Wednesday, 6 March 2003. All agenda items should be submitted to the co-chairs no later than 14 February 2003.

<signed>	<signed>
DANIEL D. REMUND	TERRANCE EGLAND
COL, MS, USA	CDR, MC, USN
Co-chair	Co-chair

APPENDIX A: BISPHOSPHONATE CLINICAL EFFICACY: CLINICAL TRIAL RESULTS

Table 1

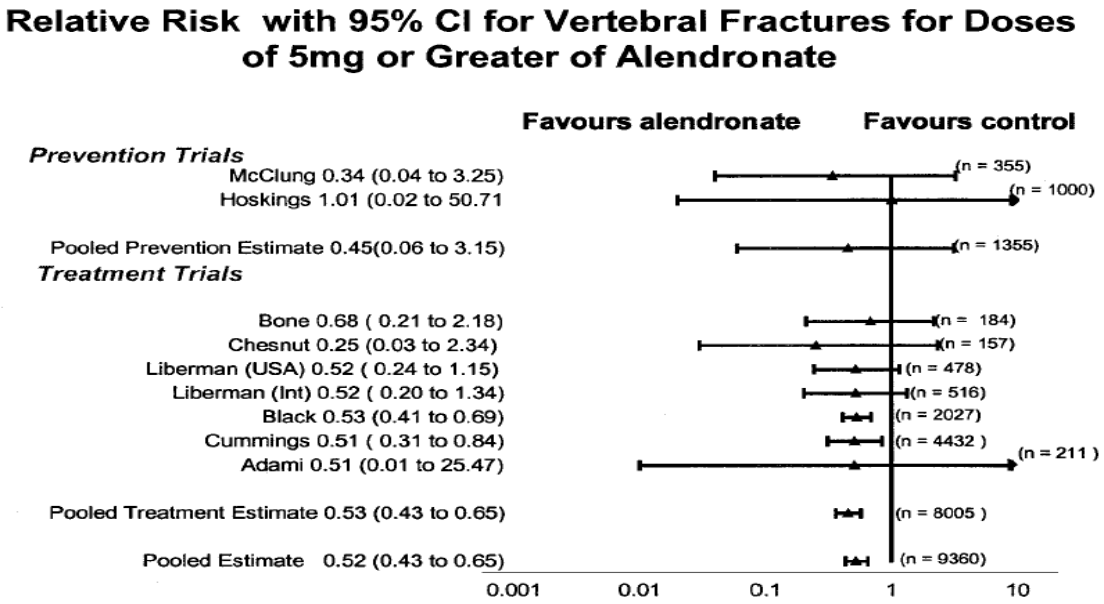


FIG. 2. RR for vertebral fractures with alendronate (5 mg and greater).

From Cranney et al; Endocrine Reviews 2002; 23(4):508-516

Table 2

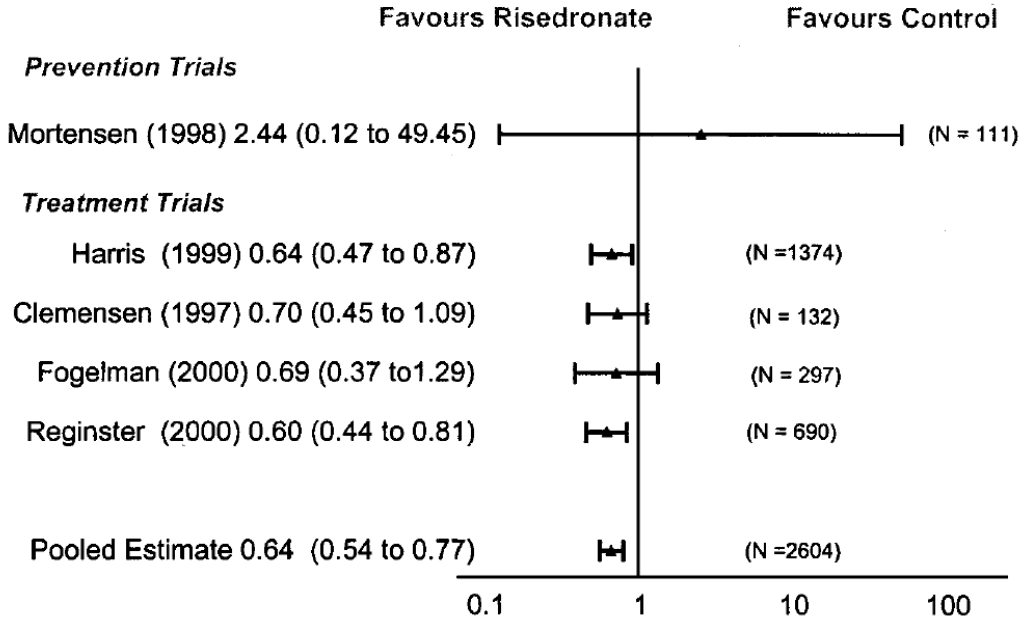


FIG. 2. Relative risk with 95% CI for vertebral fractures after treatment with risedronate.

From: Cranney et al; Endocrine Reviews 2002; 23(4):517-523

Table 3

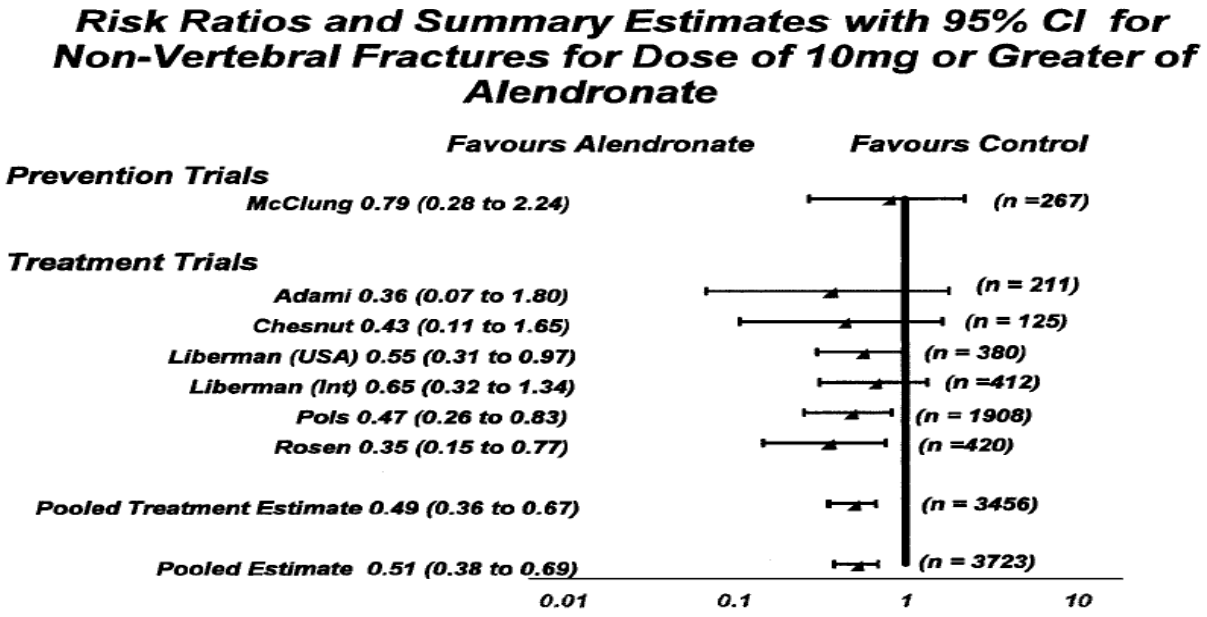


FIG. 3. Risk ratios for nonvertebral fractures with alendronate (10 mg and greater).

From: Cranney et al; Endocrine Reviews 2002; 23(4):508-516

Table 4

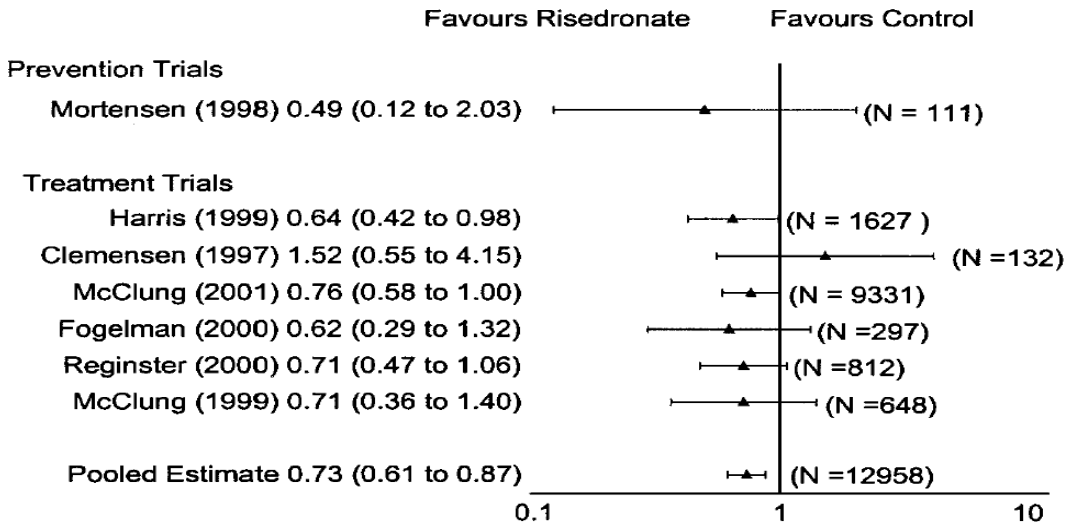


FIG. 3. Relative risk with 95% CI for nonvertebral fractures after treatment with risedronate.

From: Cranney et al; Endocrine Reviews 2002; 23(4):517-523

Table 5 – Summary of Reviewed Bisphosphonate Clinical Trials for Hip Fracture Outcomes

Study*	N	Incidence**	% Risk Reduction	Absolute Risk Reduction	NNT	Significance
Cummings [A] - 4yrs	4,432	A: 0.9% P: 1.1%	18%	0.002	500	No (P=0.44)
Liberman [A] – 3yrs	994	A: 0.2% P: 0.8%	75%	0.006	200	Not powered
Black [A] – 3yrs	2,027	A: 1.1% P: 2.2%	50%	0.011	91	Yes (P=0.047)
McClung [R] – 3 yrs	9,331	R: 2.8% P: 3.9%	28%	0.011	91 (29-333)	Yes (all) (P=0.003)
Harris [R] – 3yrs	1,628	R: 1.5% P: 1.8%	17%	0.003	333	Not powered
Reginster [R] – 3 yrs	814	R: 2.2.% P: 2.7%	19%	0.005	200	Not powered

* Lead author's last name, active component ([A]=alendronate and [R]=risedronate) and study duration
** A=Alendronate, R=Risedronate, P=Placebo

Adapted from Bolognese; The Endocrinologist 2002; 12:29-37

APPENDIX B: PROSTAGLANDIN CLINICAL EFFICACY - HEAD-TO-HEAD COMPARISON TRIALS

Table 1: Latanoprost vs. Unoprostone

Trial	Study Design	Latanoprost	Unoprostone	Duration	N	Baseline IOP (SEM)		End point IOP Reduction1 (SEM)	
						L	U	L	U
Tin Aung 2001	Randomized double-masked crossover	0.005% once daily	0.12% twice daily	2 tx periods of 1 month separated by a 3 week washout period	56	22.3 (0.5)	23.2 (0.4)	6.1 (0.5) p<.001	4.2 (0.4) p<.001

L = latanoprost, U = unoprostone, IOP = intraocular pressure
The difference of 1.9 mmHg between treatments was statistically significant in favor of latanoprost (p = .003, ANCOVA)

Table 2: Latanoprost vs. Travoprost

Trial	Study Design	L	TR	T	Duration	N	Mean Baseline IOP			Mean End point IOP		
							L	TR	T	L	TR	T
Netland 2001	Randomized multicenter, double-masked active-controlled, parallel	0.005% once daily n = 194	0.0015% n = 201 and 0.004% n = 196 once daily	O.5% Twice daily N = 196	12 months	787	25.7	25.1 (0.0015%) 25.5 (0.004%)	25.7	18.7	18.6 (0.0015%) 18.6 (0.004%)	20.2

L = Latanoprost, TR = Travoprost, T = timolol, IOP = intraocular pressure
Baseline and end point IOP difference between timolol and travoprost was statistically significant for both strengths (p<0.001, ANOVA)
Baseline and end point IOP difference between travoprost (both strengths) and latanoprost were statistically insignificant at alpha = 0.05

Table 3: Latanoprost vs. Bimatoprost

Trial	Study Design	L	B	Duration	N	Mean Baseline IOP Range		Mean End point IOP	
						L	B	L	B
Gandolfi 2001	Randomized multicenter, investigator-masked, parallel group trial	0.005% n = 113 once daily	0.03% n = 119 once daily	Three month	232	22.4 to 25.7	22.6 to 25.7	17.4 to 18	17 to 17.5
Trial	**Study Design**	**L**	**B**	**Duration**	**N**	**8 AM Mean Baseline IOP (SEM)**		**Reduction in IOP from baseline at day 29**	
						L	**B**	**L**	**B**
DuBiner 2001	Multicenter, double-masked, randomized, clinical trial	0.005% n = 21 once daily	0.03% n = 21 once daily	30-days	63	25.2 (0.6)	25.6 (0.5)	4.4 – 7.6 20-30%	5.9 – 8.0 25.4–30.9%
		Vehicle n = 21				Vehicle 25.8 (0.6)		Vehicle -0.3 – 1.7 -2 – 6.5%	

L = latanoprost, B = bimatoprost, IOP = intraocular pressure
Gandolfi: Mean IOP was lower with bimatoprost than with latanoprost at all time points (8AM, 12, 4PM, 8PM) during the three month follow-up, although the between group difference was not always statistically significant.
DuBiner: Bimatoprost and latanoprost significantly lowered IOP from baseline (p<0.001). Bimatoprost lowered IOP more than latanoprost at every time point measured, although the between group differences did not reach statistical significance.

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Pharmacoeconomic Center

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MCCS-GPE **8 AUGUST 2002**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee Meeting

1. A meeting of the DoD P&T Committee convened at 0800 hours on 8 August 2002, at the Uniformed Services University of the Health Sciences, Bethesda, Maryland

2. VOTING MEMBERS PRESENT

CDR Terrance Egland, MC, USN	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS, USA	DoD P& T Committee Co-chair
COL Mike Heath, MS (Representing MAJ Brett Kelly, MS)	Army Pharmacy Consultant Chair, DoD Pharmacy Board of Directors
Col Bill Sykora, MC	Air Force
COL Ardis Meier, BSC (Representing LtCol George Jones, BSC)	Air Force Pharmacy Consultant
CAPT (select) Matt Nutaitis, MC	Navy
CDR Kevin Cook, MSC	Navy
CAPT Robert Rist	Coast Guard
Dick Rooney	Department of Veterans Affairs

VOTING MEMBERS ABSENT

COL Rosa Stith, MC	Army
Col John R. Downs, MC	Air Force
LTC (P) Joel Schmidt, MC	Army

OTHERS PRESENT

COL William Davies, MS, USA	DoD Pharmacy Program Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
CAPT Joe Torkildson, MC, USN	DoD Pharmacoeconomic Center
LtCol Ed Zastawny, USAF, BSC	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC, USN	DoD Pharmacoeconomic Center
Maj Barb Roach, USAF, MC	DoD Pharmacoeconomic Center
LCDR Ted Briski, MSC, USN	DoD Pharmacoeconomic Center
HM1 Lisa Drumm, USN	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
David Bretzke	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
Paul Vasquez	Defense Supply Center Philadelphia
David Chicoine	Uniformed Services Family Health Plan
Mark Petruzzi	Medco Health
Ron McDonald	Sierra Military Health Services
Kelly Lenhart	Humana
William Hudson	Humana
Gene Lakey	TriWest
Ray Nan Berry	Health Net Federal Services
Trevor Rabie	Uniformed Services Family Health Plans (USFHP)

3. **REVIEW MINUTES OF LAST MEETING / ADMINISTRATIVE ISSUES** – The minutes from the last meeting were accepted as written.

4. **INTERIM DECISIONS** – No interim decisions.

5. **UNIFORM FORMULARY (UF) PROPOSED RULE**- COL Davies reported that the comment period for the UF proposed rule has closed. The TMA Pharmacy Program Office is currently in the process of formulating responses to comments submitted by the public.

6. **BCF AND NATIONAL MAIL ORDER PHARMACY (NMOP) FORMULARY ISSUES** – The Committee determined the NMOP formulary status, NMOP or retail network formulary restrictions (quantity limits or prior authorization), and Basic Core Formulary (BCF) status for 5 new drugs or formulations (see Appendix A). The PEC also presented brief information on six additional new drugs or formulations not felt to require a complete review by the Committee. The Committee agreed that no further review was required (see Appendix B for comments).

7. NMOP AND RETAIL NETWORK ISSUES

A. Clarification of the NMOP quantity limits for antibiotics – LtCol Ed Zastawny (PEC) reported on a re-evaluation of the 30-day quantity limit that the DoD P&T Committee established in July 1998 for antibiotics dispensed through the NMOP. The Committee agreed that providers are unlikely to prescribe large quantities of antibiotics unless the patient needs long-term antibiotic therapy. The 30-day quantity limit increases the administrative burden for patients with a legitimate need for long-term antibiotic therapy because they have to reorder medication more frequently. More frequent reordering of medication also increases the risk that patients will run out of medication. Patients' costs are higher because they have to pay more copays.

The Committee concluded that the 30-day quantity limit probably creates more problems than it prevents and unanimously voted to eliminate the 30-day quantity limit on antibiotics in the NMOP. Antibiotics will be dispensed according to the general rule applied to other drugs in the NMOP (up to a 90 day supply). Existing quantity limits for specific antibiotics will remain in force. All quantity limits will be posted on the quantity limit page on the PEC website.

B. Clarification of the NMOP quantity limits for myeloid stimulants, interferon gamma, interferon alpha, and sandostatin injection – The current NMOP quantity limit for these products is 30 days. Because literature supports chronic use of the interferons and sandostatin for specific indications, the Committee unanimously voted to remove the 30-day quantity limit from interferon alpha, interferon gamma, and sandostatin. The Committee agreed that a 30-day quantity limit on myeloid stimulants was reasonable given the products' indications and uses. They noted that the NMOP quantity limit for PEG-filgrastim was set at 2 syringes per 45-day supply at the May 2002 meeting. The Committee voted to retain the 30-day quantity limit for myeloid stimulants, except for PEG-filgrastim, which will remain as 2 syringes per 45-day supply limit. The quantity limits will be posted on the PEC website quantity limit page. The NMOP will not use quantity limits other than those listed on the PEC website and will revise their database(s) accordingly.

C. Clarification of NMOP quantity limits for testosterone transdermal patches (Androderm) – Current NMOP quantity limit for Androderm patches is 30 days. Testosterone topical gel (Androgel) has a NMOP quantity limit of 90 days. Both are chronic replacement products with low abuse potential. The Committee voted unanimously to remove the 30-day quantity limit on all topical/transdermal testosterone or androgen replacement products.

8. COST AVOIDANCE FROM NMOP PRIOR AUTHORIZATIONS (PAs) –Shana Trice reported on the estimated cost avoidance due to PAs in the NMOP. The cost avoidance per prescription is based on the cost avoidance model that was outlined in the Aug 00 DoD P&T Committee minutes. The Committee did not make any changes to these PAs.

Drug	2nd Quarter FY 02	3rd Quarter FY 02
Sildenafil	$11.54	-$7.79
COX-2 inhibitors	$4.10	$2.65
Etanercept	$62.84	$15.30
Anakinra	-	$1132.00

Note: Cost avoidance due to the PA for antifungals for onychomycosis (ciclopirox, itraconazole, terbinafine) is not calculated using this model because the PA differs substantially from the other PAs. Unlike the other PAs, which authorize dispensing of new and refill prescriptions for a year, each course of therapy with antifungal medications for the treatment of onychomycosis goes through the PA process.

9. SUBCOMMITTEE REPORT: PROVISION OF INJECTABLE DRUGS IN THE NMOP OR RETAIL NETWORK PHARMACIES – At the May 2002 meeting the Committee asked the PEC to analyze the prescriptions filled in the retail network for injectable drugs to determine if there were additional drugs that should be added to the NMOP Covered Injectables List. CAPT Torkildson reported on the results of that analysis.

A report was generated from PDTS listing all prescriptions filled for injectable drugs in the retail network and at the NMOP during the period 1 April 2001 – 3 May 2002. Prescriptions for drugs currently included on the NMOP Covered Injectables List were then excluded. Remaining prescriptions were then sorted based on volume of prescriptions filled and total cost to the government. The greatest volume of prescriptions filled for non-list items was for methotrexate, with 3,072 prescriptions filled over 12 months. No other non-listed medication had greater than 1,000 prescription fills. In contrast, over 39,000 prescriptions for NPH insulin, which is on the covered injectables list, were filled at retail pharmacies during the surveyed period. The drug with the highest total submitted cost due was colistimithate, with a total due of $65,792. Only colistimithate and hydromorphone had costs greater than $50,000. In contrast, the retail network cost for epoetin alpha, which is on the covered injectables list, was almost $5.9 million over the same period.

The Committee decided to add dihydroergotamine 1 mg/ml, heparin sodium 5,000 & 10,000 units/ml, and promethazine 25 mg/ml to the NMOP Covered Injectables List. Because other migraine medications are subject to quantity limits and because use of dihydroergotamine should not exceed 6 ampules per week for safety reasons, the Committee established a quantity limit for dihydroergotamine: 3 boxes (30 ampules) per 30 days in the retail network and 9 boxes (90 ampules) per 90 days in the NMOP.

The Committee also recognized that a substantially greater opportunity for cost avoidance hinged on a more aggressive use of the NMOP by patients and providers to fill prescriptions for injectable drugs already available at the NMOP.

10. **CONTROLLED DISTRIBUTION OF PRESCRIPTION DRUGS** – All the Managed Care Support Contractors have established network agreements with CVS Procare Specialty Pharmacy, making CVS Procare the preferred site for DoD patients to obtain drugs requiring controlled distribution. The current plan is to use CVS Procare, whenever possible, for future drugs requiring controlled distribution. Information about specific drugs is available on the PEC website.

11. **ADJOURNMENT –** The meeting adjourned at 1100 hours. The next meeting will be held at the Uniformed Services University of the Health Sciences, Bethesda, Maryland starting at 0800 on Thursday, 21 November 2002. All agenda items should be submitted to the co-chairs no later than 18 October 2002.

<signed>
DANIEL D. REMUND
COL, MS, USA
Co-chair

<signed>
TERRANCE EGLAND
CDR, MC, USN
Co-chair

List of Appendices

APPENDIX A: NEWLY APPROVED DRUGS CONSIDERED FOR THE NATIONAL MAIL ORDER PHARMACY FORMULARY AND DOD BASIC CORE FORMULARY

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP and/or retail network formulary restrictions**	**BCF Status**
Voriconazole (Vfend; Pfizer)	29 May 02; Treatment of invasive aspergillosis primarily due to *Aspergillus fumigatus* and treatment of serious fungal infections caused by *Scedosporium apiospermum* and *Fusarium spp*., including *Fusarium solani* in patients intolerant of, or refractory to, other therapy.	Oral 50 mg and 200 mg tablets were added to the NMOP Formulary; IV formulation was excluded (not for self-administration)	**Quantity Limits** General Rule applies **Prior Authorization:** None	Not added to the BCF **Similar BCF Drugs:** None. Fluconazole 150 mg for vaginal candidiasis has a different spectrum of activity
Etonogestrel / ethinyl estradiol vaginal ring (Nuva-Ring; Organon)	01 Oct 01; Vaginal ring composed of an estrogen and progestin indicated for the prevention of pregnancy.	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF Drugs:** None
Methylphenidate long-acting capsules (Ritalin LA; Novartis)	06 Jun 01; for the treatment of attention deficit hyperactivity disorder (ADHD) in children aged 6 to 12 years of age	Added to the NMOP Formulary **Note**: Schedule II controlled substance; would fall under standard rule in NMOP for Schedule II products for treatment of ADHD (90 days supply, no refills)	**Quantity Limits** NMOP: General rule for Schedule II controlled substances for treatment of ADHD applies. (90 days supply, no refills) **Prior Authorization** None	Not added to the BCF. Excluded from the current BCF listing for methylphenidate. **Similar BCF Drugs:** Methylphenidate extended release (Concerta)
Escitalopram (Lexapro; Forest)	Approvable at time of Committee meeting – FDA approval imminent (note: approved by the FDA 14 Aug 02); single-isomer formulation of the selective serotonin reuptake inhibitor citalopram (Celexa)	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF. Will reconsider possible BCF addition following formal FDA approval & availability of pricing information. **Similar BCF Drugs:** fluoxetine, paroxetine, sertraline, citalopram
Lovastatin extended-release tablets (Altocor; Andrx/Aura	27 Jun 02 (will not be marketed until Sept 02); indicated for use in addition to dietary restrictions to lower total cholesterol and LDL cholesterol; and to slow the progression of coronary atherosclerosis in patients with coronary heart disease. Also has indication for primary prevention of CHD in patients with elevated cholesterol (based on the AFCAPS/TexCAPS study).	Not added to the NMOP Formulary. Existence of the current statin contract precludes addition of Altocor to the NMOP formulary.	**Quantity Limits** N/A **Prior Authorization** None	Not added to the BCF. Existence of the current statin contract precludes addition of Altocor to the NMOP formulary.

APPENDIX B: NEWLY APPROVED DRUGS NOT REQUIRING FULL REVIEW BY THE P&T COMMITTEE.

Generic (Trade name; manufacturer)	**Indication**	**Comments**
Desloratadine orally disintegrating tablets (Clarinex Redi-tabs; Schering)	Treatment of allergy symptoms and chronic idiopathic urticaria	Line extension. Desloratadine tablets are already available; both formulations will be available from the NMOP. Consideration for the BCF precluded by current non-sedation antihistamine contract.
Fulvestrant for injection (IM) (Faslodex; Astra-Zeneca)	Treatment of hormone-receptor metastatic breast cancer in postmenopausal women	Not considered for the NMOP Formulary since the IM injection is not designed for self-administration.
Human insulin (rDNA origin) for injection (SC) in a 3 mL disposable prefilled syringe (InnoLet; NovoNordisk)	Human insulin (Novolin) in a 3 mL disposable prefilled syringe	Will be available from the NMOP. Existing BCF listings for Novolin insulin are for 10mL vials. MTFs may decide whether or not to add InnoLet or other alternative insulin delivery devices (e.g., insulin pens) to their formularies.
Treprostinol Na for Injection (Remodulin; United Therapeutics)	Continuous SC infusion for treatment of pulmonary hypertension with NYHA class II-IV symptoms	Restricted drug distribution
Urofollitropin for Injection (Bravelle; Ferring)	Fertility agent	Will be added to the NMOP Covered Injectables List, which already includes other brands of urofollitropin.
Ziprasidone for Injection (IM) (Geodon IM; Pfizer)	Acute episodes of paranoia, and schizophrenia	Not considered for the NMOP Formulary since the IM injection is not designed for self-administration. Emergent use agent not appropriate for the BCF.

APPENDIX C: COMBINED SUMMARY OF FORMULARY CHANGES FROM THE DOD P&T EXECUTIVE COUNCIL MEETING AND THE DOD P&T COMMITTEE MEETING

1. **BCF CHANGES**

A. Additions to the BCF

1) Venlafaxine extended release capsules (Effexor XR) - contingent on signing of BPA (see Paragraph 10A)
2) Insulin glargine injection (Lantus)
3) Gabapentin (Neurontin)
4) Budesonide inhalation solution (Pulmicort Respules)
5) Meloxicam tablets (Mobic)
6) D, L-amphetamine 10-, 20-, 30-mg extended release capsules (Adderall XR)

B. Deletions from the BCF

1) Cimetidine oral
2) Methylphenidate SR (sustained release) tablets were removed from the BCF listing for methylphenidate.

C. Changes and clarifications to the BCF

1) The current BCF listing for methylphenidate was clarified to specify the following strengths for methylphenidate extended release (Concerta): 18-, 27-, 36-, and 54-mg
2) Existing BCF listings for Novolin insulin are for 10 ml vials. MTFs may decide whether or not to add alternative insulin delivery devices (e.g., insulin pens, InnoLet) to their formularies.
3) Precision products remain the only blood glucose strips on the BCF. MTFs are encouraged to transition to the newer Precision product, Precision Extra, as soon as possible.

D. Exclusions from the BCF

1) Methylphenidate long acting capsules (Ritalin LA, Novartis) were excluded from the BCF listing for methylphenidate.
2) Lovastatin extended-release tablets (Altocor; Andrx/Aura) – existing statin contract precludes addition to the BCF

2. **NMOP FORMULARY CHANGES**

A. *Additions to the NMOP Formulary*

1) Voriconazole 50- and 200-mg tablets (Vfend; Pfizer); injectable formulation not added since it is not for self-administration
2) Etonogestrel/ethinyl estradiol vaginal ring (Nuva-Ring; Organon)
3) Methylphenidate long acting capsules (Ritalin LA; Novartis) – General NMOP rule for schedule II controlled substances for treatment of ADHD applies (90 days supply; no refills)
4) Escitalopram tablets (Lexapro; Forest)

5) Bravelle brand of urofollitropin added to the NMOP Covered Injectables List, which already includes other brands of urofollitropin

6) Dihydroergotamine 1 mg/ml injection added to the NMOP Covered Injectables List

7) Heparin sodium 5,000 & 10,000 units/ml injection added to the NMOP Covered Injectables List

8) Promethazine 25 mg/ml injection added to the NMOP Covered Injectables List

9) InnoLet brand of human insulin for injection (3 mL prefilled syringes) added to the NMOP Covered Injectables List

B. *Exclusions from the NMOP Formulary*

1) Lovastatin extended-release tablets (Altocor; Andrx/Aura) – Existing statin contract precludes addition to the NMOP Formulary.

C. *Clarifications to the NMOP Formulary* - None

3. **QUANTITY LIMIT CHANGES (NMOP AND RETAIL NETWORK)**

A. Quantity limit for dihydroergotamine 1 mg/ml injection: 3 boxes (30 ampules) per 30 days in the retail network, 9 boxes (90 ampules) per 90 days in the NMOP.

B. NMOP 30-day quantity limit for antibiotics was eliminated. Antibiotics will be dispensed consistent with the general rule applied to all other drugs in the NMOP (up to a 90 day supply), unless otherwise specified on the quantity limit page on the PEC website.

C. NMOP 30-day quantity limits for interferon alpha, interferon gamma, and sandostatin were removed. The quantity limit for myeloid stimulants remains 30 days, with the exception of PEG-filgrastim, which has a quantity limit of 2 syringes per 45 days in the NMOP, and 1 syringe per 21 days in the retail network.

D. NMOP 30-day quantity limit for topical/transdermal testosterone or androgen replacement products was removed.

4. **CHANGES TO THE PRIOR AUTHORIZATION PROGRAM (NMOP AND RETAIL NETWORK)** - None

Department of Defense
Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **7 August 2002**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Executive Council Meeting

1. The DoD P&T Executive Council met from 0800 to 1430 hours on 7 August 2002 at the Uniformed Services University of the Health Sciences, Bethesda, Maryland

2. VOTING MEMBERS PRESENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL Mike Heath, MS (Representing MAJ Brett Kelly, MS)	Army Pharmacy Consultant; Chair, DoD Pharmacy Board of Directors
COL John R. Downs, MC	Air Force
COL Bill Sykora, MC	Air Force
COL Ardis Meier, BSC (Representing LtCol George Jones, BSC)	Air Force Pharmacy Consultant
CAPT Matt Nutaitis, MC	Navy
CDR Kevin Cook, MSC	Navy
CAPT Robert Rist	Coast Guard
Dick Rooney	Department of Veterans Affairs

VOTING MEMBERS ABSENT

COL Rosa Stith, MC	Army
LTC (P) Joel Schmidt, MC	Army

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
CAPT Betsy Nolan, MSC	Navy Pharmacy Specialty Leader
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
LtCol Ed Zastawny, BSC	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC	DoD Pharmacoeconomic Center
CDR (sel) Ted Briski, MSC	DoD Pharmacoeconomic Center
LtCol Barb Roach, MC	DoD Pharmacoeconomic Center
HM1 Lisa Drumm, USN	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
Dave Bretzke	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
Paul Vasquez	Defense Supply Center Philadelphia
Alexandra Masterson, Pharm.D.	Dewitt Army Hospital, Ft. Belvoir, VA

3. REVIEW MINUTES OF LAST MEETING/ADMINISTRATIVE ISSUES

The minutes from the last meeting were accepted as written.

4. INTERIM DECISIONS – None

5. NATIONAL PHARMACEUTICAL CONTRACTS AND BLANKET PURCHASE AGREEMENTS (BPAs)

Contract awards, renewals, and terminations

- New joint DoD/VA contracts were awarded for benztropine, carbidopa/levodopa IR, famotidine, digoxin, indomethacin, metformin, captopril, paclitaxel, trazadone, and chlorhexidine.
- The following joint DoD/VA contracts were not awarded because the bid prices were higher than existing FSS prices: prednisone and cimetidine.
- The following joint DoD/VA contracts are in various stages of solicitation: penicillin, dicloxacillin, tretinoin cream, amoxicillin, and cephalexin.
- The following joint DoD/VA contracts were extended: salsalate and all Geneva generics.

6. EXPIRATION OF LISINOPRIL CONTRACT

LCDR Briski provided information concerning the availability and pricing of lisinopril within the direct care system. The DoD contract with Astra Zeneca that provided the Zestril brand of lisinopril at $0.14 per tablet expired on 31 July 2002. Astra-Zeneca refused a DoD request to extend the Zestril contract. The VA's contract with Merck for the Prinivil brand of lisinopril expires 19 October 2002. Astra-Zeneca and Merck are phasing out production of lisinopril. Although several companies market generic versions of lisinopril, none are listed on the Federal Supply Schedule, and all are priced significantly higher than $0.14 per tablet. The DoD and VA are seeking a joint contract for a generic version of lisinopril, but that contract will not be awarded until after the VA's

Prinivil contract expires. MTFs will probably have to pay higher prices for lisinopril until the contract for a generic version of lisinopril is awarded—hopefully by November 2002.

7. PENDING CONTRACT INITIATIVES

A. Status of contracting initiatives for Leutinizing Hormone Releasing Hormone (LHRH) agonists, nasal corticosteroids, triptans, and quinolones – The joint DoD/VA solicitations for these items are still pending.

B. Status of contracting initiative for Angiotensin Receptor Blockers (ARBs) – In order for DoD to potentially join the VA in seeking a closed class contract for an ARB, LCDR Briski asked the Council to reconsider its May 2002 decision that the procurement strategy must leave the ARB class "open" on the BCF. The Council's decision not to support a closed class contract centered on concerns about therapeutic interchangeability and clinical coverage for treating congestive heart failure (CHF) and preventing the progression of renal disease in type 2 diabetics.

The Council considered new information about the extent to which ARBs are prescribed at MTFs for conditions other than hypertension. An analysis of data from the Uniformed Services Prescription Database (USPD) and the M2 (formerly known as the ARS Bridge) database found ICD-9 codes consistent with a diagnosis of CHF or type 2 diabetic renal disease for only 289 (5%) of 5,680 patients who were prescribed two or more daily doses of an ARB (Note: patients with CHF are more likely to be prescribed multiple daily doses of an ARB than patients who are being treated for hypertension). The Council concluded that a closed class contract would be acceptable because the usage of ARBs for these conditions is low enough that MTFs could use the non-formulary request process to provide non-contracted ARBs to patients in the event that the contracted ARB does not meet the clinical needs of patients with CHF or type 2 diabetes. The Council voted unanimously to expand the authorized procurement strategies for the ARB class to include a closed class contract that does not mandate that patients be switched from non-contracted ARBs to the contracted ARB.

C. Status of contracting initiative for thiazolidinediones (TZDs, "glitazones") – In order for DoD to potentially join the VA in seeking a closed class contract for a TZD, LCDR Briski asked the Council to reconsider its May 2002 decision that the procurement strategy must leave the TZD class "open" on the BCF. The Council's decision not to support a closed class contract stemmed from concerns that rosiglitazone and pioglitazone may differ significantly in their effects on LDL-cholesterol (LDL-C) levels. The Council considered the results of (1) a more extensive analysis of changes in LDL-C levels reported in clinical trials of TZDs, and (2) an analysis of concomitant statin therapy for DoD patients who were newly started on TZD therapy.

Comparison of changes in LDL-C levels in clinical trials of TZDs: There are no head-to-head trials that compare the changes in LDL-C levels that are associated with the use of rosiglitazone and pioglitazone. In order to compare the changes in LDL-C levels while attempting to control for known and unknown variations that exist across clinical trials of TZDs, the PEC calculated the percentage change in LDL-C incremental to placebo in nine rosiglitazone trials and five pioglitazone trials. As shown in Tables 1 and 2 below, the incremental percentage increases in LDL-C are consistently larger for rosiglitazone than pioglitazone.

Table 1: Monotherapy trials with TZDs and corresponding LDL changes, incremental to placebo

Rosiglitazone				Pioglitazone			
Dose (N)	**Base-line LDL**	**% change in LDL**	**% change incremental to placebo**	**Dose (N)**	**Base-line LDL**	**% change in LDL**	**% change incremental to placebo**
Patel				Aronoff			
2 mg bid (79)	125	↑ 13.6%	**↑ 12.4%**	30 mg qd (87)	136	↑ 5.2%	**↑ 0.42**
Placebo (74)	130	↑ 1.2%		Placebo (79)	139	↑ 4.8%	
Lebovitz				Study 026			
2 mg bid (166)	121	↑13.7%	**↑ 8.9%**	30 mg qd (100)	126	↓ 7%	**↓ 7%**
Placebo (158)	121	↑ 4.8%		Placebo (93)	133	No change	
Phillips				Study 012			
2 mg bid (186)	130	↑ 9.5%	**↑ 7.8%**	30 mg qd (85)	123	↑ 7%	**↑ 1%**
Placebo (173)	127	↑ 1.7%		Placebo (83)	135	↑ 6%	
Phillips							
4 mg qd (181)	125	↑ 10.6%	**↑ 8.9%**				
Placebo (173)	127	↑ 1.7%					
Lebovitz				Aronoff			
4 mg bid (169)	124	↑ 18.6%	**↑ 13.8%**	45 mg qd (80)	127	↑ 6%	**↑ 1.2%**
Placebo (158)	121	↑ 4.8%		Placebo (79)	139	↑ 4.8%	
Phillips				Study 012			
4 mg bid (187)	135	↑ 14.3	**↑ 12.6%**	45 mg qd (85)	133	↑ 8%	**↑ 2%**
Placebo (173)	127	↑ 1.7%		Placebo (83)	135	↑ 6%	
Phillips							
8 mg qd (181)	129	↑ 18.3%	**↑ 16.6%**				
Placebo (173)	127	↓ 1.7%					

Table 2: TZD trials in combination with a sulfonylurea or metformin and corresponding LDL changes, incremental to placebo

Rosiglitazone				Pioglitazone			
Dose (N)	**Base-line LDL**	**% change in LDL**	**% change incremental to placebo**	**Dose (N)**	**Base-line LDL**	**% change in LDL**	**% change incremental to placebo**
Wolffen				Kipnes			
2 mg bid +SU (183)	139	↑ 6%	**↑ 6%**	30 mg qd +SU (189)	127	↑ 6.6%	**↓ 0.4%**
Placebo + SU (192)	139	No change		Placebo +SU (187)	124	↑ 7%	
Study 079							
2 mg bid + glyb (98)	125	↑ 10.4%	**↑ 10.2%**				
Glyb (99)	125	↑ 0.24%					
Study 079							
2 mg bid (99)	125	↑ 17.6%	**↑ 17.4**				
Glyb (99)	125	↑ 0.24%					
Study 096							
4 mg qd + glyb (116)	122	↑ 14.8%	**↑ 12.4%**				
Placebo (115) + glyb	122	↑ 2.4%					
Fonesca*				Einhorn*			
4 mg qd + met (119)	115	↑ 15.4%	**↑ 12%**	30 mg qd +met (161)	119	↑ 7.7%	**↓ 4.2%**
Met + placebo (116)	117	↑ 3.4%		Placebo +met (149)	118	↑ 11.9%	
Fonesca*				No combination trials with 45 mg pioglitazone			
8 mg qd + met (113)	112	↑ 18.7%	**↑ 15.3%**				
Met + placebo (116)	116	↑ 3.4%					

SU = sulfonylurea, glyb = glyburide, met = metformin
*Concomitant lipid-lowering drugs were allowed

Analysis of concomitant statin therapy among DoD patients newly started on TZD therapy: Using data from the Pharmacy Data Transaction Service (PDTS), the PEC identified 14,301 patients who began therapy with rosiglitazone or pioglitazone between 1 November 2001 and 28 February 2002 and analyzed their concomitant statin usage through 30 June 2002. The PEC identified patients who had received prescriptions for statins before starting their TZD therapy, patients who initiated statin therapy after starting TZD therapy, and patients who experienced an increase in the dosage of their pre-existing statin therapy. Table 3 shows that the percentages of patients who were on statin therapy at baseline, were started on a statin, or whose statin dose was increased are very similar for rosiglitazone and pioglitazone.

Table 3: Statin use in DoD patients newly started on TZDs

	Rosiglitazone (n=8369)	Pioglitazone (n=5932)
Statin therapy change	**2120 (25.3%)**	**1371 (23.1%)**
Statin started after TZD started	1702 (20.3%)	1103 (18.6%)
Statin dose increased	418 (5%)	268 (4.5%)
No statin therapy change	**6249 (74.7%)**	**4561 (76.9%)**
No statin prescription	3606 (43.1%)	2641 (44.5%)
Statin dose not increased	2643 (31.6%)	1920 (32.4%)

Conclusion: While the data from clinical trials suggest that rosiglitazone is associated with larger increases in LDL-C than pioglitazone, concomitant usage of statins by DoD patients is very similar for both drugs. The Council voted 8-2 to expand the authorized procurement strategies for the TZD class to include a closed class contract that does not mandate that patients be switched from a non-contracted TZD to a contracted TZD.

D. *Status of contracting initiative for statins* – The Council reviewed recent label changes for simvastatin (Zocor) that Merck voluntarily initiated with the FDA as a result of normal post-marketing surveillance and monitoring of ongoing clinical trials. The label changes approved by the FDA on 6 June 2002 further clarify the risk of myopathy and rhabdomyolysis, particularly with higher doses of simvastatin and when used with other drugs. Myopathy and rhabdomyolysis are well-known side effects of all statins. The revised label includes the following:

- *Concomitant use with fibrates and niacin (≥1g/day)* – simvastatin dose should not exceed 10 mg daily unless the benefit outweighs the increased risk.
- *Concomitant use with amiodarone or verapamil* – simvastatin dose should not exceed 20 mg daily unless the benefit outweighs the increased risk. In a clinical trial, 6% of patients taking amiodarone and simvastatin 80 mg daily developed myopathy. Combined clinical trial data showed a 0.6% risk of myopathy with simvastatin (20-80 mg) and verapamil.
- *Dose-related risk of myopathy/rhabdomyolysis* – the incidence in clinical trials, in which patients were carefully monitored and some interacting drugs were excluded, has been approximately 0.02% at 20 mg, 0.07% at 40 mg & 0.3% at 80 mg.

The Council noted that a recent Clinical Advisory on the Use and Safety of Statins from the National Heart, Lung, and Blood Institute, the American College of Cardiology, and the American Heart Association states that a review of data regarding reports of fatal rhabdomyolysis among the different statins strongly suggests that there are no clinically important differences in the rate of

fatal complications among the five statins now available in the U.S., and that clinicians should consider the rates of severe myopathy as equivalent among these statins.

The Council unanimously concluded that the simvastatin label change is not cause to alter its previous decision to support any contracting/formulary strategy (to include a closed class contract) that places at least one high potency statin on the BCF and does not require patients to be switched from one agent to another.

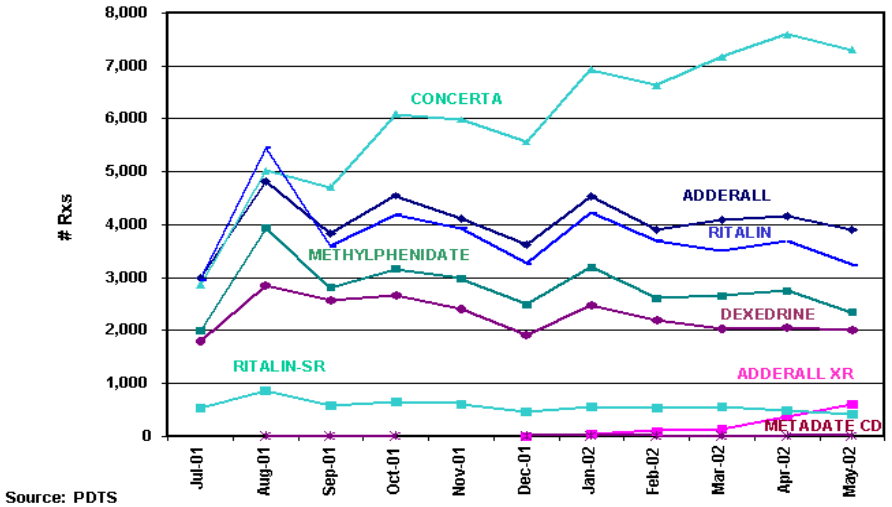
8. DRUG CLASS EVALUATIONS TO DETERMINE CLINICALLY ACCEPTABLE CONTRACTING/FORMULARY STRATEGIES:

A. *Attention Deficit Hyperactivity Disorder (ADHD) stimulant medications* — Based on a recommendation from the PEC, the Council reviewed the list of stimulant medications currently included on the BCF for the treatment of ADHD. The stimulants most widely used for ADHD treatment are methylphenidate, dextroamphetamine, and mixed salts of amphetamine/dextroamphetamine. Methylphenidate is available in immediate-release, sustained-release, and extended release forms. Dextroamphetamine is available in immediate and extended release forms, while the mixed salts of amphetamine/dextroamphetamine are available in sustained release (Adderall and generics) and extended release (Adderall XR) forms. The three agents currently on the BCF are all methylphenidate products: methylphenidate immediate release, methylphenidate sustained release, and Concerta. Pemoline is another stimulant medication used for ADHD, but its side effect profile is not acceptable to most clinicians. Pemoline is reserved as a last-line therapy when all other treatments have failed, and was not considered further in this review.

Therapeutic interchangeability/clinical coverage: There appear to be two subsets of ADHD patients: those who respond to methylphenidate and those who respond to amphetamine products. According to the literature, initial treatment of ADHD with a stimulant medication from a particular class has approximately a 65% likelihood of success. A substantial number of treatment failures can be successfully treated with the alternate drug class. Which class is used first is largely a matter of prescriber preference, as there are no clinical features that predict which class of drugs is more likely to be successful for a given patient. Given these facts, a health system should have products and dosage forms from both the methylphenidate and amphetamine classes available to meet the clinical needs of its ADHD patients. Once a class of drugs is found to be effective, current practice guidelines for the treatment of ADHD recommend that patients be changed to an extended release formulation to enhance compliance, decrease the risk of drug diversion within the school setting, and minimize the stigma associated with school-age children taking midday doses of stimulants. Therefore, optimal management of ADHD requires the availability of both methylphenidate and amphetamine products, and requires that preference be given to dosage forms that minimize the likelihood that patients will need to take additional doses of medication during the school day.

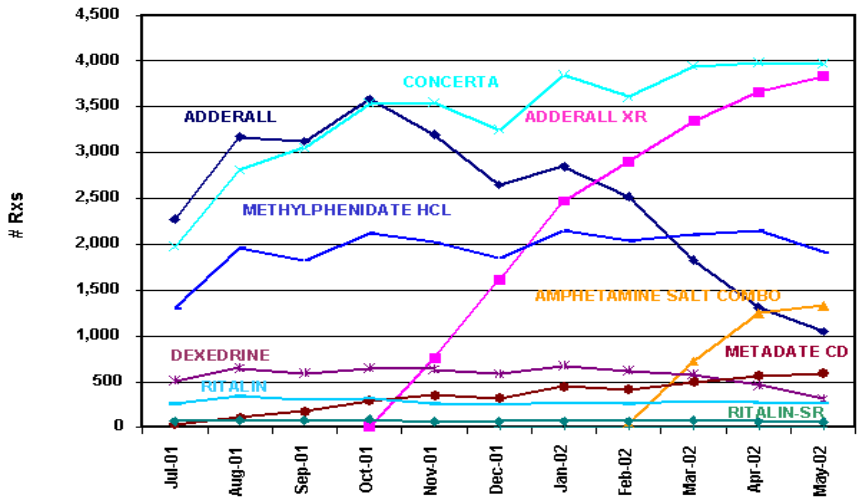
Utilization: The utilization trends within the MTFs and retail network pharmacies are presented in Figures 1 and 2.

Figure 1: MTF Prescriptions for ADHD Stimulant Medications (Jul 01 – May 02)



Source: PDTS

Figure 2: Retail Network Prescriptions for ADHD Stimulant Medications (Jul 01 – May 02)



Source: PDTS

Concerta is the most commonly dispensed stimulant medication at MTFs, with Adderall currently in second place. This is in sharp contrast to the retail network, where Concerta is also the most commonly dispensed drug, but Adderall XR is in second place and rapidly gaining ground. It is also noteworthy that use of Ritalin SR is very low in both points of service, despite its current position on the BCF. The retail network utilization trends (where all products are uniformly available) support the contention that methylphenidate and amphetamine products should both be available for the provision of comprehensive care to patients with ADHD, and also show that providers preferentially select the extended release formulation of these products for long-term therapy.

Provider acceptance: There was strong support among DoD providers who treat children with ADHD for a more robust BCF with broadened clinical coverage for ADHD patients. More than half of the respondents felt that an amphetamine product (Adderall or Adderall XR) should be added to the BCF to improve clinical coverage. Providers indicated that they would not favor any procurement strategy that resulted in a closed class with a single entity or required patients to be switched from one drug class to another. Most physicians felt that parents would be very resistant to medication changes mandated by contract once their child was being effectively treated with a particular medication. All agreed that pemoline is not a candidate for the BCF due to its side effect profile.

Based on this review, the Council approved the following decisions:

- Retain Concerta and methylphenidate IR on the BCF.
- Remove methylphenidate SR from the BCF
- Add Adderall XR 10-, 20- and 30-mg strengths to the BCF. Facilities may add additional strengths if they desire, but they are not mandated to do so.

9. DRUG/DRUG CLASS EVALUATIONS TO DETERMINE BCF ADDITION

A. *Venlafaxine extended release capsules (Effexor XR)* – In February 2002 the Council reviewed the anxiolytic class and concluded that venlafaxine extended release (Effexor XR; Wyeth-Ayerst) was useful in the treatment of several anxiety disorders, particularly in patients with co-morbid depression. A decision to add venlafaxine extended release to the BCF was tabled at that time pending discussions with the company intended to increase the cost-effectiveness of this therapy. Consideration was deferred again in May, as discussions with the company were still ongoing. Subsequently, the company presented a verbal offer of a $0.10 per tablet price reduction on the 150 mg tablet in return for BCF status.

Table 4: Current FSS pricing of Effexor/Effexor XR:

Drug	Strength	Price/tablet	Cost/30 days
Effexor	25 mg	$0.57	$34.20
	37.5 mg	$0.60	$35.76
	50 mg	$0.61	$36.84
	75 mg	$0.66	$39.30
	100 mg	$0.69	$41.52
Effexor XR	37.5 mg	$1.06	$31.80
	75 mg	$1.19	$35.70
	150 mg	$1.29	$38.70

Given the current rate of growth in utilization of venlafaxine extended release, the MHS would likely realize a cost avoidance of over $200,000 annually by accepting this offer. More savings are possible if BCF addition facilitates MTF recapture of venlafaxine extended release prescriptions from the retail network. The Council voted unanimously to add venlafaxine extended release 37.5, 75, and 150 mg tablets to the BCF, contingent on the signing of a BPA between Wyeth-Ayerst and DSCP establishing the $0.10 price reduction for the 150 mg tablet.

B. *Insulin glargine (Lantus)* – The Council considered a proposal to add insulin glargine (Lantus; Aventis Pharmaceuticals) to the BCF. Insulin glargine is a modified human insulin designed to act as a peakless basal insulin product with a 24-hour duration of action. It was approved by the FDA in April 2000 but was not launched until May 2001. The major advantage of insulin glargine is an approximately 10% lower incidence of symptomatic hypoglycemia, nocturnal

hypoglycemia, and severe hypoglycemia compared to NPH insulin. Initial studies suggested that the efficacy of insulin glargine in reducing HbA_{1c} levels was equivalent to that of NPH. Other brief trials demonstrated a significant decrease in the fasting plasma or whole blood glucose levels compared to NPH. Abstracts presented at the most recent American Diabetes Association meeting suggested that the enhanced safety profile of insulin glargine allows for a more aggressive approach to escalating insulin therapy in both Type 1 and Type 2 diabetics, and that this more aggressive approach in fact leads to a significant decrease in HbA_{1c} levels compared to traditional therapy with NPH insulin.

Even though insulin glargine costs much more than human NPH insulin at MTF pharmacies ($25.38 versus $4.49 per 10 ml vial) and is currently on fewer than half of MTF formularies, the prescription volume for insulin glargine increased 3.5 fold at MTF pharmacies between October 2001 and May 2002. Prescription volume for insulin glargine increased 2.5 fold in the retail network during the same period.

The Council concluded that insulin glargine represents a true advance in the treatment of both Type 1 and Type 2 diabetes and that it should be uniformly available at MTF pharmacies. The Council voted unanimously to add insulin glargine to the BCF.

C. *Gabapentin (Neurontin)* – In February 2002 the Council reviewed gabapentin for potential addition to the BCF, due to high usage rate and high expenditures in the retail network. The Council decided not to add gabapentin at that time due to concern that gabapentin was not FDA approved for pain control and that it may pose a large cost burden to small MTFs. The FDA recently approved gabapentin for treatment of post herpetic neuralgia. A generic version of gabapentin may become available in the near future. In the retail network gabapentin is in the top 20 for expenditures and top 50 for number of prescriptions. Gabapentin is among the top 100 drugs for number of prescriptions in the MTFs and is on 70% of MTF formularies. Gabapentin usage has continued to rise in all three points of service, with the majority of use for neuropathic pain in the over-65 aged population. The Council voted unanimously to add gabapentin to the BCF.

10. CLARIFICATION OF STATUS OF BLOOD GLUCOSE TEST STRIPS ON BCF – Precision (Abbott) blood glucose test strips have been on the BCF since its inception. Precision's status on the BCF is supported by an incentive price agreement that offers a lower price system-wide as market share increases. A medical/surgical product standardization initiative for TRICARE Regions 6, 7 and 8 recently selected the Accucheck (Roche Diagnostics) blood glucose test strip. Some pharmacies were incorrectly told that they had to switch from Precision test strip to the Accucheck test strip. LCDR Briski wrote an article in the May edition of the *PEC Update* and also disseminated information through the service pharmacy consultants/specialty leaders to MTF pharmacies to clarify that Precision test strips remain on the BCF and that regional medical/surgical standardization initiatives do not create "sole source" agreements that force MTFs to switch away from an item listed on the BCF.

The Army serves as the Executive Agent for medical/surgical regional standardization. The Council agreed that COL Remund should meet with COL Kissane, the Army OTSG/MEDCOM Deputy Chief of Staff for Logistics, to work out some rules of engagement that would enable national standardization through the BCF and regional standardization initiatives to productively coexist.

LCDR Briski also briefed the Council about Abbott Diagnostic's plan to phase out the Precision QID strip and meter, while phasing in their newer product, Precision Extra. The Precision Extra

product offers significant advancements over the Precision QID product. The Council voted to reaffirm its intent to keep Precision products as the sole blood glucose strip on the BCF. The Council encourages MTFs to expeditiously transition to the Precision Extra product.

11. CLARIFICATION OF 27- AND 54-MG STRENGTHS OF METHYLPHENIDATE EXTENDED RELEASE (CONCERTA) – When Concerta was first added to the BCF in November 2000, the only strengths available were 18 mg and 36 mg. A 54 mg capsule was marketed in December 2000, and a 27 mg capsule was added in April 2002. Multiple strengths allow more precise titration of dosages. During a recent PEC review of Concerta utilization at MTFs, it was noted that several large MTFs were dispensing a large number of dual prescriptions to patients for both 18 mg and 36 mg Concerta capsules rather than for 54 mg capsules. This results in an inconvenience to the patient, an increase in workload for the pharmacy, and an excess cost of $38.40 per patient per month.

To facilitate dosage titration and to maximize the likelihood that Concerta will be used in as cost-effective a manner as possible, the Council voted to add the 27 mg and 54 mg strengths of Concerta to the BCF. The vote was 8 in favor, one against, and one abstention.

12. MTF REQUESTS FOR BCF CHANGES

A. Requests to delete particular strengths or dosage forms of BCF items – The Health Affairs Policy for Basic Core Formulary and Committed Use Requirements Contracts (Policy #98-034) states, “In the case of multiple strength BCF drugs, all strengths need not be stocked but all prescriptions for that agent will be filled regardless of strength.” The BCF page on the PEC website explains that a listing for an oral medication “indicates all oral dosage forms and strengths will be provided unless otherwise noted.” The DoD P&T Executive Council has deleted or excluded some dosage forms/strengths from the BCF for one or more of the following reasons:

- Substantially higher cost than other dosage forms/strengths
- Excessive administrative burden associated with maintaining multiple strengths (e.g., controlled substances)
- The BCF listing is intended to cover an indication that is limited to a specific dosage form/strength (e.g., fluconazole 150 mg for vaginal yeast infections)
- New dosage form/strength offers no significant clinical advantage and is apparently designed to avert competition from generic versions of the drug
- Low usage combined with one or more of the factors above

Some MTF requests to delete a particular strength or dosage form of a BCF drug appear to be based primarily on objections to stocking an item that has a low usage rate. The Council reiterates that if an MTF has little or no demand for a particular BCF item, the MTF is not required to physically stock the item in the pharmacy. However, the MTF must provide the item if it is prescribed.

B. *Request to remove cimetidine from the BCF* – A MTF pharmacist requested the deletion of cimetidine from the BCF due to low usage. Cimetidine and ranitidine are the two H2 blockers currently on the BCF. Ranitidine prescriptions outnumber cimetidine prescriptions 9 to 1 at MTF pharmacies. Indications and efficacy are similar for both drugs, but cimetidine has more side effects and drug interactions than ranitidine. Ranitidine costs $0.06 - $0.07 per day; cimetidine costs $0.10 to $0.13 per day. The Council voted unanimously to delete cimetidine from the BCF. MTFs may decide to retain cimetidine on their local formularies if so desired.

C. *Request to remove cyproheptadine from the BCF* –An MTF pharmacist requested deletion of cyproheptadine from the BCF because there are better alternatives on the BCF to treat allergies and headache and because cyproheptadine had been dispensed fewer than 20 times in the past 6 months at the requestor's MTF. More than 90 responses were received from providers and pharmacists in the field, overwhelmingly and convincingly offering reasons why this drug should be maintained on the BCF in spite of low usage. Cyproheptadine has a unique place in therapy with no good alternative treatments for pregnant patients and young children with migraine headaches, in addition to other uses. The 4 mg tablet is priced as low as $0.03 per tablet, and the 2 mg per 5 ml syrup costs $0.15 per 5 ml. The Council voted unanimously to retain cyproheptadine on the BCF.

D. *Request to remove theophylline elixir from the BCF* –An MTF pharmacist requested deletion of theophylline oral liquid from the BCF because it has been dispensed less than 20 times in the past 6 months at the requestor's MTF. Children and elderly patients who cannot swallow solid dosage forms or are unable to use a metered-dose-inhaler effectively account for almost all of the theophylline oral liquid use. Theophylline remains on asthma and COPD treatment guidelines, and the oral liquid form is the only dosage form that is suitable for some patients. Theophylline oral liquid is inexpensive ($0.003 to $0.045 per ml). The Council voted unanimously to retain theophylline oral liquid on the BCF.

E. *Request to add budesonide inhalation suspension (Pulmicort Respules) to the BCF* – A pediatrician requested addition of budesonide inhalation suspension to the BCF for the following reasons: 1) it is the only FDA-approved, nebulized steroid available and can be used for patients as young as 12 months of age; 2) prior to the availability of budesonide inhalation suspension, steroid metered dose inhalers (MDIs) were used for persistent asthmatics—young children could not always cooperate effectively with these; 3) parents appreciate the convenience of nebulized medications in children and studies have shown them to be efficacious; and 4) one in nine children has asthma—addition would enhance primary care options for treatment.

   The safety and tolerability of nebulized budesonide are no different than other inhaled steroids. Both inpatient and outpatient studies have shown efficacy in respect to symptom relief. As expected, use of this medication is low and almost exclusively for patients in the 0 to 4 age group, which is consistent with appropriate use of the product. MDIs are still the inhaled steroid formulation of choice in the treatment of asthma. Budesonide inhalation suspension is intended for those who cannot yet use MDIs appropriately. The Council voted unanimously to add budesonide inhalation suspension (Pulmicort Respules) to the BCF.

F. Request to add meloxicam (Mobic) to the BCF – The PEC received two requests to add meloxicam to the BCF, one from an Air Force physician and one from an Army pharmacist. Both requestors represent facilities currently using meloxicam as an alternative to "COX-2 inhibitors" (rofecoxib, celecoxib, or valdecoxib).

The Council considered the following points:

- *Background* - Meloxicam is FDA-approved only for osteoarthritis (OA). Because patent protection/exclusivity for meloxicam is expected to expire within the next three years, the manufacturer has stated that they do not plan to pursue additional indications. The drug is approved in various European countries for rheumatoid arthritis (RA). Despite its relatively recent introduction in the U.S. in April 2000, meloxicam has been available in other countries since 1995. The manufacturer estimates that more than 45 million patients have been exposed to meloxicam worldwide.
- *Efficacy* - There are published clinical trials showing efficacy of meloxicam for the treatment of OA, RA, and other chronic painful conditions, including ankylosing spondylitis and low back pain. Publication of the IMPROVE trial, a 6-month naturalistic (effectiveness) trial in OA patients (meloxicam vs. "usual care" NSAIDs) is expected shortly; summary results are available in abstract.
- *Safety –NSAID-associated GI adverse events*
  - *COX-2 selectivity* - The most extensive analysis of COX-2/COX-1 selectivity of NSAIDs to date (Warner et al. Proc Nat Acad Sci 1999; 96:7563-8) constructed the following ranking based on a whole blood assay (from most COX-2 selective to least COX-2 selective): rofecoxib (>50-fold COX-2 selective); etodolac, meloxicam, and celecoxib (grouped together as 5-to 50-fold COX-2 selective); diclofenac, sulindac, piroxicam, ibuprofen, tolmetin, naproxen, aspirin, indomethacin, ketoprofen, ketorolac. According to other researchers, the COX-2 selectivity of meloxicam appears to be dose-related, with greater COX-2 selectivity at a daily dose of 7.5 mg than at 15 mg.
  - *Association of COX-2 selectivity with reduced incidence of serious upper GI events* - The major potential advantage of COX-2 selective NSAIDs relative to non-selective NSAIDs is a reduction in the incidence of complicated upper GI events (GI bleed, perforation, and obstruction) and symptomatic but uncomplicated ulcers. Evidence of a reduced incidence of complicated upper GI events compared to nonselective NSAIDs is most conclusive with rofecoxib, less conclusive with celecoxib and meloxicam, and not yet available for valdecoxib. Because no head-to-head trials of sufficient size and duration to discern a clinically significant difference in complicated upper GI events are available, it is difficult to compare the incidence rate of complicated upper GI events with meloxicam and celecoxib, rofecoxib, or valdecoxib. See Appendix A for a discussion of clinical studies involving meloxicam, celecoxib, and rofecoxib.
- *Safety: Cardiorenal and cardiovascular adverse events* - NSAIDs, including celecoxib, rofecoxib, and valdecoxib, are known to cause fluid retention, edema, blood pressure (BP) elevation, and loss of BP control in patients treated with antihypertensive medications. In addition, the VIGOR trial with rofecoxib showed a statistically significantly higher incidence of adjudicated serious cardiovascular thrombotic events (primarily acute myocardial infarctions) in patients treated with rofecoxib 50 mg QD compared to patients treated with naproxen 500 mg BID [1.1% vs. 0.5%, NNH=167].

Pooled data from the Meloxicam Serious GI Event Analysis, which includes clinical trial data involving 27,039 patients who received meloxicam, comparator NSAIDs, or placebo in 35 clinical trials, provides comparative information on the incidence of these adverse events in patients treated with meloxicam or comparator NSAIDs (see Table 5). Placebo data included in this analysis are very limited (736 patients, 113 patient-years of therapy) and are not included in the table because they are unlikely to accurately reflect background rates.

Table 5: Rates of cardiovascular/cardiorenal adverse events

	Meloxicam	NSAIDs
Patients	15,071	11,078
Patient-years of therapy	3129	1202
Myocardial Infarctions (incidence/100 pt-yrs)	18 (0.58%)	8 (0.67%)
Cardiac Failure (incidence/100 pt-yrs)	15 (0.48%)	7 (0.58%)
Peripheral Edema (incidence/100 pt-yrs)	98 (3.13%)	79 (6.57%)
Hypertension (incidence/100 pt-yrs)	82 (2.62%)	32 (2.66%)
Aggravated HTN (incidence/100 pt-yrs)	25 (0.80%)	15 (1.25%)

- *Tolerability* - Meloxicam appears to be as well or better tolerated than the NSAIDs to which it was compared in clinical trials. In the MELISSA study, fewer patients treated with meloxicam withdrew from the study due to GI adverse effects (e.g., dyspepsia, nausea, abdominal pain) compared with diclofenac (3.0% vs. 6.1%); similar results were observed in the SELECT trial (3.8% vs. 5.3% with piroxicam). Preliminary results from the IMPROVE study show significantly fewer discontinuations of therapy due to adverse effects compared to “usual care” NSAIDs.
- *Other Factors*
  - *Frequency of Dosing* - Meloxicam is dosed once daily.
  - *Provider Input* - The PEC requested provider (physician and pharmacist) input on this issue. Because the VA has selected etodolac for their COX-2 criteria as an alternative to salsalate for patients at significant GI risk, and because etodolac, like meloxicam, has at least some evidence of a lower incidence of GI adverse events than other NSAIDs, providers were asked about etodolac as well as meloxicam. Providers were asked: 1) if their MTF would use meloxicam or etodolac if added to the BCF, 2) the place of the drug(s) in therapy, 3) should meloxicam or etodolac be added to the BCF, and 4) how addition would affect their facility. The responses were mixed. Key points included:
    - One responder pointed out that while BCF addition would probably have a significant budgetary impact on facilities that currently have no COX-2s on formulary, the overall cost to DoD should drop significantly if these facilities would call civilian providers and switch COX-2 prescriptions to meloxicam, preventing a significant number of COX-2 prescriptions from being filled in the network at a higher overall cost to DoD. MTFs that currently do not have COX-2 inhibitors on formulary may incur increased costs.
    - Some responders were concerned that if meloxicam were added to formularies without restrictions, providers may shift from prescribing lower cost generic NSAIDs to prescribing meloxicam, even in patients at low risk for GI adverse events.

  - Some responders doubted that providers would use meloxicam or etodolac in place of rofecoxib or commented that these are low use items at their facilities.
  - Some responders commented that there was insufficient clinical trial evidence to conclude that meloxicam is COX-2 sparing.
  - With regard to etodolac, responders commented that while it is generically available and less costly than meloxicam and there is some evidence that it is COX-2 sparing; it must be dosed 2-3 times per day and is not actively marketed to providers. Comments about the effectiveness of etodolac ranged from "good success" to "useless" (and must, in any case, be regarded as anecdotal).

- *Status on MTF formularies* - Facilities that currently have meloxicam on formulary (either unrestricted or as part of a step therapy program that requires failure of one or more nonselective NSAIDs prior to meloxicam) include: Tripler Army Regional Medical Center (ARMC); Madigan ARMC; Brooke Army Medical Center, Wilford Hall Medical Center, Randolph Air Force Base (AFB); Ft. Polk; Luke AFB; Ft. Hood; Ft. Leonard Wood; William Beaumont ARMC; and Nellis AFB.
- *Dose distribution - MTFs vs. retail network* - Since the COX-2 selectivity of meloxicam appears to be dose-related, the percentage of patients receiving 7.5- vs. 15-mg daily doses is of interest. As of July 2002, about 80% of meloxicam prescriptions filled in the NMOP and retail network were for the 7.5-mg strength of meloxicam, which is consistent with the 80-85% reported by the manufacturer as typical in the civilian marketplace. Only about 35% of meloxicam prescriptions filled at MTFs were for the 7.5 mg strength; however, the true percentage of MTF meloxicam prescriptions written for a 7.5-mg daily dose is likely to be closer to 65% due to splitting of the 15-mg tablet (see following analysis).
- *Cost*
  - *Dose distribution and MTF cost per day* - The PEC analyzed signatura (directions for use) for all MTF prescriptions for meloxicam, celecoxib, rofecoxib, and etodolac with valid signatura in the Uniformed Services Prescription Database from Jan – April 2002 (134,883 Rxs). This analysis served two purposes: to analyze the dose distribution of meloxicam and to compare the weighted average cost per day of meloxicam to the COX-2 inhibitors and to etodolac. Valdecoxib was not included due to the limited number of MTF prescriptions during this time period.

Table 6: Dose distribution and weighted average daily cost

Generic	Strength / dosage form	Daily dose (# tabs/caps per day)	% of Rxs	Average cost per tab/cap purchased by MTFs	Weighted average daily cost
Meloxicam	15 mg tab	0.5 1	39.6% 34.6%	$0.97	$0.80*
	7.5 mg tab	1 2	19.5% 5.9%	$0.88	
Celecoxib	100 mg cap	1 2	5.9% 15.8%	$0.80	$1.76
	200 mg cap	1 2	54.2% 23.2%	$1.45	
Rofecoxib	12.5 mg tab	1	7.6%	$1.35	$1.43
	25 mg tab	1 2	71.5% 5.9%	$1.37	
	50 mg tab	0.5 1	6.5% 5.7%	$2.13	
Etodolac	200 mg cap	2	2.0%	$0.15	$0.52
	300 mg cap	2 3	8.4% 2.3%	$0.20	
	400 mg tab	1 2 3 4	2.6% 70.4% 6.8% 2.2%	$0.27	

Based on all prescriptions with valid signatura (directions for use) in the Uniformed Services Prescription Database Jan – April 2002 and the average price per tab/cap purchased by MTFs, based on prime vendor data for Apr – May 02. Rows representing less than 2% of all prescriptions for a specific medication are omitted; percentages may not add to 100% for this reason. Usage of extended release etodolac was extremely low and is not reflected in these results.
* Results for meloxicam reflect a high percentage of prescriptions for meloxicam 15 mg tabs as 0.5 tabs per day, most likely due to tablet-splitting. In the absence of tablet-splitting strategies (i.e., substitution of 7.5 tabs for all 15 mg half-tabs), the weighted average cost per day would be about $0.96.

- The manufacturer has offered DoD a blanket purchase agreement for meloxicam. The BPA provides a price reduction from $0.89 to $0.79 for the 7.5 mg tab and from $0.98 to $0.88 for the 15 mg tab, a reduction of about 11%, in return for placing meloxicam on the BCF. The BPA would be effective no later than Oct 2002 and run through 31 Dec 2003. The BPA does not prevent later addition of a COX-2 inhibitor or any other NSAID to the BCF. Using the same method described above, these price decreases would reduce the weighted average daily cost of meloxicam from $0.80 to $0.73 per day.

The Council agreed that the evidence for a GI-sparing effect with meloxicam is not as certain as that for rofecoxib, but that there is sufficient evidence to conclude that meloxicam is associated with fewer serious GI events than the less COX-2 selective NSAIDs with which it has been compared in clinical trials. The Council emphasized that because meloxicam is still substantially more costly than generic NSAIDs (e.g., naproxen, ibuprofen, diclofenac), it does not make sense to use meloxicam in patients at low risk of GI events.

It is difficult to accurately predict whether addition of meloxicam to the BCF will result in greater cost (if meloxicam is used in place of generic NSAIDs) or cost avoidance (if meloxicam is used in place of celecoxib, rofecoxib, or valdecoxib). One large Army MTF that previously had celecoxib and rofecoxib on formulary with a criteria-based prospective medication use evaluation form deleted celecoxib and rofecoxib from their formulary and added meloxicam after discovering that a majority of the patients receiving celecoxib or rofecoxib did not meet criteria. After 4 months, they reported substantial cost avoidance, no adverse drug reactions, no new drug requests for celecoxib or rofecoxib as a result of treatment failures, and a 100% conversion rate when outside providers were contacted requesting a change to meloxicam.

The Council voted to add meloxicam (Mobic) to the BCF. The Council agreed that facility-level guidelines or programs to ensure appropriate use of meloxicam, as well as celecoxib, rofecoxib, or valdecoxib, are consistent with BCF policy as long as the guidelines are applied uniformly and consistently (e.g., to both military and civilian providers).

The Council also considered addition of etodolac to the BCF, but decided that it did not have sufficient data concerning the clinical utility and GI-sparing effect of etodolac and tabled the issue to a later date.

G. *Request to add aspirin/extended release dipyridamole (Aggrenox) to the BCF* – Two providers, a neurologist and a neuro-ophthalmologist, requested that Aggrenox (aspirin 50 mg/extended release dipyridamole 200 mg) be added to the BCF. Aggrenox is indicated to reduce the risk of stroke in patients who have had transient ischemia of the brain or completed ischemic stroke due to thrombosis. Aggrenox does not have approval for coronary heart disease. The 1999 AHA guidelines for the Management of TIA identify Aggrenox as an acceptable option for initial therapy following a TIA, along with aspirin, clopidogrel and ticlopidine. All have been shown to reduce the risk of recurrent stroke in patients who have had a TIA. Clopidogrel is indicated for reduction of thrombotic events in patients with recent stroke or established peripheral arterial disease, and is also indicated for use in unstable angina or myocardial infarction. Clopidogrel was added to the BCF in February 2002

Safety and tolerability of Aggrenox are similar to the two separate ingredients used in combination, with headache as the major limitation. The European Stroke Prevention Study-2 (ESPS-2) was the major efficacy trial for Aggrenox. Dropout rates in the Aggrenox and dipyridamole groups of the ESPS-2 were significantly higher than those reported in the aspirin and placebo groups. The high overall dropout rate (26%) raises the question of poor patient compliance.

There is no conclusive evidence that Aggrenox offers a significant advantage over the concomitant use of aspirin and dipyridamole to reduce the risk of stroke. The relative risk reduction for aspirin and dipyridamole versus placebo in the ESPS-1 study (38.1%) was similar to the relative risk reduction for Aggrenox versus placebo in the ESPS-2 study (37.2%).

Aggrenox is significantly more expensive than using separate tablets of aspirin or dipyridamole together. Aggrenox costs $1.76/day, which is similar to clopidogrel at $1.80/day. PDTS usage data from July 2001 – June 2002 showed there were only 2000 Aggrenox prescriptions vs. 20,000 clopidogrel prescriptions in the entire DoD.

Only 25 responses were obtained from providers regarding potential BCF addition of Aggrenox, of whom 20 were against BCF addition. Aggrenox has minimal usage in DoD, is not supported by the primary care providers, and does not offer clear benefit over clopidogrel. The Council voted not to add Aggrenox to the BCF. Individual MTFs may add Aggrenox to their local formulary if desired.

13. ADJOURNMENT

The meeting adjourned at 1430 hours on 7 August 2002. The next meeting will be held at the Uniformed Services University of the Health Sciences, Bethesda, Maryland starting at 0800 on Wednesday, 20 November 2002. All agenda items should be submitted to the co-chairs no later than 18 October 2002.

<signed>	<signed>
DANIEL D. REMUND	TERRANCE EGLAND
COL, MS, USA	CDR, MC, USN
Co-chair	Co-chair

Appendix A: Studies Indicating a Reduced Incidence of Complicated Upper GI Events with Rofecoxib, Celecoxib, or Meloxicam

Abbreviations used in this appendix: absolute risk reduction (ARR); confidence intervals (CI); relative risk (RR), number-needed-to-treat (NNT); number-needed-to-harm (NNH)

Rofecoxib

- The VIGOR trial (Bombardier et al. N Engl J Med 2000; 343:1520-8) compared rofecoxib and naproxen in 8000+ RA & OA patients. The median duration of the trial was 9 months; patients on aspirin were excluded. This trial provides the best evidence to date that a COX-2 selective NSAID results in fewer complicated upper GI events (perforations, obstructions, or upper GI bleeds) and symptomatic ulcers. The incidence of confirmed complicated upper GI events was 0.6% in the rofecoxib group vs. 1.4% with naproxen [absolute risk reduction (ARR) = 0.8%, relative risk (RR) = 0.43 (95% CI 0.24-0.78), p=0.005, number needed to treat (NNT) = 125], while the incidence of the combined endpoint of confirmed complicated upper GI events **or** symptomatic ulcers was 2.1% with rofecoxib vs. 4.5% with naproxen [ARR=2.4%, RR=0.46 (95% CI 0.33-0.64), p<0.001, NNT=41].

Celecoxib

- The CLASS trial (Silverstein et al. JAMA 2000; 284:1247-55) compared celecoxib vs. a pooled NSAID group (ibuprofen or diclofenac) in 8000+ OA patients. The duration of the trial was approximately 13 months (6-month results published); patients on prophylactic aspirin were included. Published (6-month) data from the CLASS trial reported fewer confirmed complicated upper GI events with celecoxib vs. pooled NSAIDs, but the difference was not statistically significant [0.76% celecoxib vs. 1.45% NSAIDs; ARR 0.69%; RR=0.53 (95% CI 0.26-1.11), p=0.09]. A statistically significant difference was found for the combined endpoint of complicated upper GI events **or** symptomatic ulcers [2.08% celecoxib vs. 3.54% NSAIDs; ARR 1.46%; RR=0.59 (95% CI 0.38-0.94), p=0.02]. About 22% of patients were receiving low-dose aspirin. A subgroup analysis of patients not receiving aspirin resulted in significant results for celecoxib vs. pooled NSAIDs for both endpoints; there were no differences between celecoxib and pooled NSAIDs in patients receiving low-dose aspirin.

  Subsequent to initial publication, FDA briefing documents and reviews (available at www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1.htm) were made available addressing the entire duration of the trial. When the entire 13-month study period was considered, there was no significant difference between celecoxib and the pooled NSAID group for the primary endpoint of confirmed complicated UGI events in the overall study population, the subgroup of patients not receiving aspirin, or the subgroup of patients receiving aspirin. The differences in statistical significance between six-month data and data from the entire study period appeared to be due to the occurrence of relatively more confirmed complicated UGI events in the celecoxib group than in NSAID groups subsequent to the first six months (see Table 7).

Table 7: Number of confirmed complicated UGI events in the CLASS trial
(uncensored intent-to-treat data)

	Celecoxib (n=3987)	Diclofenac (n=1996)	Ibuprofen (n=1985)
First 6 months	11	9	11
Entire Study Period	17	10	11

Adapted from Tables 13 and 14, Medical Officer Review for Celebrex®, available at: *www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1_03_med.doc*

FDA briefing documents and reviews also provide separate data for the two comparator NSAIDs, which was not available in the published report. All differences that were statistically significant between celecoxib and the pooled NSAID group were significant for celecoxib versus ibuprofen. Regardless of aspirin use, there was no difference between diclofenac and celecoxib in any endpoint.

Meloxicam

- Two large (8000+ patient) meloxicam safety trials have been published, SELECT (Dequeker et al. Brit J Rheumatol 1998; 37:946-51) and MELISSA (Hawkey et al. Brit J Rheumatol 1998; 37:937-45). Each of the two 28-day trials randomized patients with OA to meloxicam or a comparator NSAID (piroxicam in SELECT and diclofenac in MELISSA); the trials were otherwise of identical design. The choice of NSAID comparators facilitated comparison of results with meloxicam vs. both a relatively COX-1 selective NSAID (piroxicam) and a relatively COX-2 selective NSAID (diclofenac). In SELECT, 7 patients treated with meloxicam had complicated upper GI events or ulcerations compared to 16 patients treated with piroxicam. All four cases involving perforations or bleeding occurred with piroxicam. In MELISSA, 5 patients treated with meloxicam had complicated upper GI events or ulcerations compared to 7 patients treated with diclofenac. Although both comparisons were statistically nonsignificant, the numerical results are consistent with the known COX-2 selectivity of the comparators.
- While meloxicam lacks a GI safety study comparable in size and duration to VIGOR or CLASS, summary results of large pooled analyses of clinical trial data are becoming available. Summary results of a pooled analysis of meloxicam clinical trial data involving 27,039 patients who received meloxicam, comparator NSAIDs, or placebo in 35 clinical trials have been published in abstract by Dr. Singh and colleagues, and are available from the manufacturer as the "Meloxicam Serious GI Event Analysis." (Note: multiple abstracts concerning this analysis are available at www.eular.org; search 2001 & 2002 abstracts for "meloxicam.")
- An analysis of complicated upper GI events (perforations, obstructions, or clinically serious upper GI bleeds) per 100 patient-years in patients who received placebo, various doses of meloxicam, diclofenac, or piroxicam during meloxicam clinical trials is shown in the table below (Singh G, Triadafilopoulos G. European Congress of Rheumatology, June 2001. Abstract SAT0085). The rate of complicated upper GI events with meloxicam appeared to be dose-related and lower than rates with diclofenac or piroxicam.

Table 8: Rate of complicated UGI events & NNH

Drug	N	Cumulative pt-yrs	Events	Events per 100 pt-yrs	NNH*
Placebo	736	113	0	0	-
Mel 7.5 mg	10158	918	3	0.3	333
Mel 15 mg	2960	1451	9	0.6	167
Mel 22.5	910	600	6	1.0	100
Diclofenac	5464	524	9	1.7	59
Piroxicam	5371	603	16	2.7	37

NNH = number-needed-to-harm to cause 1 additional event compared to placebo

- Preliminary results from an even larger pooled analysis are available in abstract (Furst et al, European League Against Rheumatism 2002, Stockholm, Sweden. Abstract THU0264, available online at www.eular.org). The analysis included data from 48 clinical trials including 117,755 patients with rheumatic diseases who received meloxicam, comparator NSAIDs, or placebo during meloxicam clinical trials. Cumulative hazards (95% CI) after 3 months for complicated upper GI events (perforations, obstructions, or GI bleeds) was: 0.05% (0-0.12%) for meloxicam 7.5 mg; 0.42% (0.12-0.71%) for meloxicam 15 mg; estimate for diclofenac 0.51% (0.16-0.86%); estimate for piroxicam 1.11% (0.35-1.88%).

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Pharmacoeconomic Center

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MCCS-GPE **8 MAY 2002**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee Meeting

1. A meeting of the DoD P&T Committee convened at 0800 hours on 8 May 2002, at the Commissioned Officers Club, Fort Sam Houston, TX

2. MEMBERS PRESENT

CDR Terrance Egland, MC, USN	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS, USA	DoD P& T Committee Co-chair
Col John R. Downs, MC	Air Force
Col Mark Nadeau, MC (For Col Bill Sykora, MC)	Air Force
LtCol George Jones, BSC	Air Force
CAPT (select) Matt Nutaitis, MC	Navy
CDR Kevin Cook, MSC	Navy
LTC (P) Joel Schmidt, MC	Army
MAJ Brett Kelly	Army
CAPT Robert Rist	Coast Guard
Dick Rooney	Department of Veterans Affairs
LTC Mike Kieffer, MS	Joint Readiness Clinical Advisory Board
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
William Hudson	Humana
Gene Lakey	TriWest
Ray Nan Berry	Health Net Federal Services
Trevor Rabie	Uniformed Services Family Health Plans (USFHP)

MEMBERS ABSENT

COL Rosa Stith, MC	Army
Ron McDonald	Sierra Military Health Services

OTHERS PRESENT

COL William Davies, MS, USA	DoD Pharmacy Program Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
CAPT Joe Torkildson, MC, USN	DoD Pharmacoeconomic Center
LTC Don DeGroff	DoD Pharmacoeconomic Center
LtCol Ed Zastawny, USAF, BSC	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC, USN	DoD Pharmacoeconomic Center
Maj Barb Roach, USAF, MC	DoD Pharmacoeconomic Center
LCDR Ted Briski, MSC, USN	DoD Pharmacoeconomic Center
SFC Agustin Serrano	DoD Pharmacoeconomic Center
HM1 Lisa Drumm	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
David Bretzke	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
Paul Vasquez	Defense Supply Center Philadelphia
David Chicoine	Uniformed Services Family Health Plan
Mark Petruzzi	Merck-Medco
Elizabeth Scaturro	Merck-Medco Managed Care
David Spiler	Merck-Medco
CAPT Howard Hays	USPHS/Indian Health
CAPT Samuel Hope	USPHS/Indian Health
CAPT Robert Pittman	USPHS/Indian Health
LCDR Thomas Berry	USPHS/Indian Health

3. **REVIEW MINUTES OF LAST MEETING / ADMINISTRATIVE ISSUES** – The minutes from the last meeting were accepted as written.

4. **INTERIM DECISIONS** – COL Remund reported on interim decisions:

   - Interferon beta 1a (Rebif) was added to the NMOP covered injectables list because interferon beta 1a (Avonex) and interferon beta 1b (Betaseron) were already included on the list.
   - In response to safety concerns raised by the FDA, Roche Laboratories implemented the System to Manage Accutane Related Teratogenicity (SMART) program on 10 April 02. The SMART program includes prescribing restrictions that make it infeasible for the NMOP to continue to fill Accutane prescriptions, so Accutane was removed from the NMOP Formulary.

5. **UNIFORM FORMULARY (UF) PROPOSED RULE**- COL Davies presented an extensive description of the UF proposed rule. The UF Proposed Rule was posted on the following website: http://frwebgate.access.gpo.gov/cgi-bin/multidb.cgi; Federal Register, Vol 67, No 71, FRI 12 Apr 2002; Civilian Health and Medical Program of the Uniformed Services. The proposed rule will be open to public comment until 11 June 2002. Comments may be submitted by email to: uniformulary@tma.osd.mil.

6. **ACADEMY OF MANAGED CARE PHARMACY (AMCP) FORMAT FOR FORMULARY SUBMISSIONS** – The AMCP developed the Format for Formulary Submissions in order to (1) improve the timeliness, quality, scope, and relevance of information available to P&T committees, and (2) streamline the data acquisition and review process for managed care organization staff pharmacists. The Format requires pharmaceutical companies to construct "dossiers" that provide drug information in a standardized format. Each dossier contains the following sections: product information, supporting clinical and economic information, an impact model report (to predict system-wide consequences of formulary changes), clinical value and overall cost, supporting information. COL Remund reported that the PEC will ask pharmaceutical companies to submit dossiers on new agents. Use of the AMCP Format will hopefully reduce the burden on the PEC staff for compiling drug information and allow more time for analyzing the information.

7. **BCF AND NATIONAL MAIL ORDER PHARMACY (NMOP) FORMULARY ISSUES** – The Committee determined the NMOP formulary status, NMOP or retail network formulary restrictions (quantity limits or prior authorization), and Basic Core Formulary (BCF) status for 7 new drugs or formulations (see Appendix A).

8. **REEVALUATION OF SILDENAFIL (VIAGRA) POLICY** – Tabled until the meeting in August 02.

9. **NMOP AND RETAIL NETWORK ISSUES**

   A. Clarification of the "line extension rule" for the NMOP Formulary – Shana Trice (PEC) reported on the current process for determining the formulary status of new formulations and dosage forms of medications that are already on the NMOP Formulary. Non-injectable medications in the following categories are added to the NMOP Formulary without formal action by the DoD P&T Committee unless the NMOP contractor and the NMOP Contracting Officer's Technical Representative (COTR) identify a reason for the P&T Committee to be involved in the decision:

   a. Generic equivalent of an agent already on the NMOP formulary
   b. New dosage form of an agent already on the NMOP formulary
   c. New formulation of an agent already on the NMOP formulary
   d. New drug entity in a therapeutic class/category for which the Committee has previously approved automatic inclusion for new drug entities. Currently the only drug class to which this applies is AIDS/HIV drugs. The Committee will review drugs automatically included under this provision at the next scheduled meeting.

   New combination products of non-injectable medications that are already on the NMOP Formulary are added to the NMOP Formulary only upon the decision of the P&T Committee or by the co-chairs through the interim decision mechanism. This does not apply to therapeutic classes/categories in which the Committee has previously approved automatic inclusion for new drug entities (i.e., AIDS/HIV drugs).

   The Committee agreed that the current process is working and should be retained, but emphasized that the preceding categories should be applied as guidelines rather than absolute rules. If Merck-Medco personnel and the NMOP COTR agree that further review is warranted for any reason, the issue should be referred to the PEC for further investigation and a recommendation for the co-chairs and/or the Committee.

The Committee agreed that the same guidelines could be applied to addition of injectable medications to the NMOP Covered Injectables List, since Merck-Medco personnel and the NMOP COTR will look at new dosage forms, formulations, and combination products and will refer issues to the PEC for further review as needed.

B. Clarification of the NMOP quantity limits for antibiotics – Subsequent to a patient question regarding a quantity limit on an antibiotic prescription filled through the NMOP, Lt Col Zastawny presented information regarding quantity limits on antibiotics through the NMOP.

A general 30-day quantity limit on antibiotics from the NMOP and a list of antibiotics exempted from the 30-day quantity limit rule were approved by the Committee at the July 1998 meeting (http://www.pec.ha.osd.mil/PTC/ptmin078.pdf), and posted with the July 1998 P&T minutes. This information was never published on the PEC website's quantity limit page, so most committee members, providers, and patients are unaware of the 30-day quantity limit on antibiotics or the antibiotics that were exempt from the 30-day limit. The NMOP contractor, however, has applied the 30-day quantity limit to antibiotic prescriptions filled through the NMOP. According to the NMOP COTR, antibiotic quantity limits in the NMOP have caused very few complaints over the past 3 years.

The Committee decided to table this topic until the August 2002 meeting in order to allow members time to review the antibiotic quantity limits and make informed decisions.

10. PRIOR AUTHORIZATIONS (PAs)

A. Report on PA drugs – Shana Trice (PEC) reported that all changes to NMOP PA criteria approved at the last meeting had been completed and that PA forms, criteria, and clinical rationale explanations were posted on the PEC website.

B. Proposed revision to anakinra PA criteria – Given the current shortage of etanercept, the Committee discussed revising the anakinra PA criteria to make it easier for patients unable to obtain etanercept to be started on anakinra. They decided to make no changes because it does not appear that existing etanercept patients have been unable to receive etanercept for continuation of therapy (although the NMOP reported delays of some days in supplying etanercept to patients) and because making the administrative change to NMOP PA criteria would require at least 90 days.

C. Cost avoidance from NMOP PAs – The Committee approved the recommendation to report cost avoidance of NMOP PAs at every other meeting. The next report will be at the August 02 meeting.

11. SUBCOMMITTEE REPORT: PROVISION OF INJECTABLE DRUGS IN THE NMOP OR RETAIL NETWORK PHARMACIES

– Lt Col George Jones reported that the subcommittee was uncertain about what it was supposed to do. The subsequent discussion focused on the possibility of applying the NMOP Covered Injectables List to the retail network to define what injectable products would be available from retail network pharmacies. COL Davies pointed out that the DoD P&T Committee does not have the authority to make such a decision, as this would constitute a change in the pharmacy benefit by making a group of drugs unavailable in both purchased care venues. Another committee member again stated the opinion that this was a safety issue, but the Committee felt that in general this was not the case. The Committee decided to disband the subcommittee.

The Committee subsequently considered that there may be injectable drugs being dispensed in the retail network that are not being dispensed through the NMOP that in fact could be provided through the NMOP. The PEC will use prescription data from PDTS to analyze this issue. Mr. Bill Hudson from Humana Health Care, one of the members of the original subcommittee, also expressed an interest in remaining involved with this issue. The Committee agreed with this course of action.

12. CONTROLLED DISTRIBUTION OF PRESCRIPTION DRUGS – The FDA has mandated controlled or restricted distribution mechanisms for several agents. The current status of those agents within the DoD is:

A. Schering, the manufacturer of pegylated interferon (PEG-Intron), emplaced a mechanism to allow DoD activities to order directly. Details will be available on the PEC website.

B. Pfizer, the manufacturer of dofetilide (Tikosyn), emplaced a mechanism to allow DoD activities to order directly, and the Managed Care Support Contractors are providing the drug through their retail pharmacy networks. Details will be available on the PEC website.

C. Members of the DoD Pharmacy Board of Directors are working with Roche and the FDA to establish a mechanism for Accutane to be prescribed via electronic physician order entry instead of requiring hard copy prescriptions.

D. Etanercept (Enbrel) is in short supply. Current patients' needs are being met. New patients are being placed on a waiting list. Relief is not expected soon. Providers are being advised to consider alternative therapy.

E. Actelion, the manufacture of bosentan (Tracleer), maintains five specialty distributors to distribute Tracleer. CVS Procare is one of the specialty distributors, and is part of the TRICARE retail network. All Tracleer patients should enroll into the Tracleer Access Program (TAP) by using the toll-free telephone number 866-228-3546. At that time they will be assigned to CVS Procare as their specialty pharmacy. None of the other specialty pharmacies are part of the MCSC retail pharmacy networks. Using any pharmacy other than CVS Procare would result in an out-of-network claim, which requires advance payment for the drug and the filing of a paper claim; the patient would only be reimbursed the cost of the drug minus a cost share, which is substantially greater than the network's $9.00 copay.

13. ADJOURNMENT – The meeting adjourned at 1200 hours. The next meeting will be held at the Uniformed Services University of the Health Sciences, Bethesda, Maryland starting at 0800 on Thursday, 08 August 2002. All agenda items should be submitted to the co-chairs no later than 08 July 2002.

<signed>
DANIEL D. REMUND
COL, MS, USA
Co-chair

<signed>
TERRANCE EGLAND
CDR, MC, USN
Co-chair

List of Appendices

APPENDIX A: NEWLY APPROVED DRUGS CONSIDERED FOR THE NATIONAL MAIL ORDER PHARMACY FORMULARY AND DOD BASIC CORE FORMULARY

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP and/or retail network formulary restrictions**	**BCF Status**
Pegfilgrastim injection (Neulasta; Amgen)	31 Jan 02; pegylated form of filgrastim (G-CSF) indicated to reduce the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving chemotherapy associated with a clinically significant incidence of febrile neutropenia.	**Note**: Filgrastim and Epogen are both on the NMOP covered injectables list. Added to the NMOP Formulary and Covered Injectables List	**Quantity Limits** 2 syringes per 45 day supply (NMOP); 1 syringes per 21 day supply (retail network). **Rationale for quantity limits:** Potential for excessive cost due to product wastage. **Prior Authorization:** None	Not added to the BCF **Similar BCF Drugs:** None
Comments regarding pegfilgrastim injection: Pegfilgrastim is given once per chemotherapy cycle as a single dose of 6 mg administered at least 24 hours after chemotherapy. Filgrastim is administered daily for up to 14 days following chemotherapy. Pegfilgrastim, at $1730/syringe, is somewhat more costly than a 10-day course of filgrastim at a daily dose of 300 mg per day ($1037) or 480 mcg per day ($1640). Because patients may decline further courses of chemotherapy due to unacceptable toxicity, the potential for product wastage is significant. Because pegfilgrastim should not be administered during the 14 days before chemotherapy because of the potential for an increase in the sensitivity of rapidly dividing myeloid cells to cytotoxic chemotherapy, it is not suitable for chemotherapy cycles much shorter than 21 days. A quantity limit of 2 syringes per 45 days (NMOP) or 1 syringe per 21 days (retail) allows a sufficient supply to cover the next chemotherapy cycle and a sufficient time to order the next needed dose				
Norelgestromin / ethinyl estradiol transdermal patch (Ortho-Evra; Ortho-Biotec)	20 Nov 01; prevention of pregnancy; first contraceptive available in a transdermal formulation; the ethinyl estradiol component is equivalent to 20 mcg of EE/day (low-dose estrogen). Norelgestromin is produced following oral administration of norgestimate, the progestin component found in Ortho-Cyclen and Ortho-Tricyclen.	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF Drugs:** None
Budesonide capsules (Entocort EC; Astra Zeneca)	02 Oct 01; glucocorticoid for the treatment of mild to moderate active Crohn's disease involving the ilieum and/or ascending colon (acute flares)	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF Drugs:** None

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP and/or retail network formulary restrictions**	**BCF Status**
Morphine sulfate extended release capsules (Avinza; Ligand)	20 Mar 02; launched on 2 May 02. Modified-release formulation of morphine sulfate intended for once-daily administration indicated for the relief of moderate to severe pain requiring continuous, around-the-clock opioid therapy for an extended period of time; not intended for prn use.	Added to the NMOP Formulary.	**Quantity Limits:** General rule for Schedule II controlled substances applies; limited to 30 days supply at the NMOP **Rationale for quantity limits:** Existing quantity limits for Schedule II controlled substances **Prior Authorization** None	The current BCF listing for morphine sulfate extended release was clarified to exclude Avinza. **Similar BCF Drugs:** Morphine sulfate extended release (MS Contin and generic equivalents)
Olmesartan medoxomil (Benicar; Sanyko / Forrest)	25 Apr 02; approved for hypertension. This is the 7th Angiotensin Receptor Blocker (ARB) to be approved in the U.S.	Added to the NMOP Formulary.	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF Drugs:** None
Extended phenytoin sodium, 200 mg and 300 mg capsules (Phenytek; Bertek)	6 Dec 01; new branded formulation of phenytoin sodium indicated for the treatment of generalized tonic-clonic and complex partial seizures and prevention and treatment of seizures during or following neurosurgery 200 and 300 mg Phenytek capsules are bioequivalent to 2 and 3 Dilantin 100-mg capsules, respectively	Added to NMOP Formulary as a line extension.	**Quantity Limits** General rule applies **Prior Authorization** None	The current BCF listing for phenytoin oral was clarified to exclude Phenytek. **Similar BCF Drugs:** Oral phenytoin
Paroxetine controlled-release tablets (Paxil CR; GlaxoSmithKline)**)**	Approved for depression Feb 99 but not marketed until FDA approval for panic disorder was obtained in Feb 02. This new formulation of paroxetine does NOT extend the dosing interval (once-daily); a polymer matrix controls the dissolution rate over 4-5 hours and an enteric coating delays release until tablets have left the stomach, potentially improving tolerability. Because of reduced bioavailability, Paxil CR strengths are higher (12.5-, 25-, 37.5-mg) than Paxil immediate release (10-,20-,30-,40-mg).	Added to the NMOP Formulary	**Quantity Limits:** General rule applies **Prior Authorization:** None	The current BCF listing for paroxetine oral was clarified to exclude Paxil CR, pending a more thorough review in 6 months. **Similar BCF Drugs:** paroxetine, fluoxetine, citalopram, sertraline
Comments concerning paroxetine controlled-release tablets – The Committee agreed that information concerning the potential advantages of Paxil CR compared to immediate release paroxetine was not sufficiently complete to mandate that Paxil CR be added to all MTF formularies at this time. In addition, they wanted to obtain provider opinions concerning the utility of the new formulation that were not available at the time of the meeting. Paxil CR will be reviewed again in 6 months. It will be excluded from the BCF pending review.				

APPENDIX B: COMBINED SUMMARY OF FORMULARY CHANGES FROM THE DOD P&T EXECUTIVE COUNCIL MEETING AND THE DOD P&T COMMITTEE MEETING

1. **BCF CHANGES**

A. Additions to the BCF

1) Combivent (ipratropium/albuterol sulfate) oral inhaler
2) Raloxifene (Evista)
3) Pseudoephedrine/Guaifenesin 600/120 mg extended release (Entex PSE equivalent).
4) Levonorgestrel 0.75 mg (Plan B)—added to the BCF on 3 April 2002, but subsequently deleted from the BCF on 8 May 2002.

B. Deletions from the BCF

1) Propranolol LA
2) Levonorgestrel 0.75 mg (Plan B)—deleted from the BCF on 8 May 2002

C. Changes and clarifications to the BCF

1) The current BCF listing for carbinoxamine/pseudoephedrine drops was changed to the "new" formulation (1 mg/15 mg per ml) since this is the only formulation available.

A. Exclusions from the BCF

1) Morphine sulfate extended release capsules (Avinza; Ligand)
2) Extended phenytoin sodium, 200- and 300 mg capsules (Phenytek; Bertek)
3) Paroxetine controlled-release tablets (Paxil CR; GlaxoSmithKline) – pending more thorough review in 6 months.

2. **NMOP FORMULARY CHANGES**

A. Additions to the NMOP Formulary (See Appendix A for details)

1) Pegfilgrastim injection (Neulasta; Amgen) – added to the NMOP Covered Injectables List. Quantity limits apply, see below
2) Norelgestromin/ethinyl estradiol transdermal patch (Ortho-Evra; Ortho-Biotec) –
3) Budesonide capsules (Entocort EC; Astra Zeneca)
4) Morphine sulfate extended release capsules (Avinza; Ligand)
5) Olmesartan medoxomil (Benicar; Sanyko/Forrest)
6) Extended phenytoin sodium 200- and 300 mg capsules (Phenytek; Bertek)
7) Paroxetine controlled-release tablets (Paxil CR; GlaxoSmithKline)

B. Exclusions from the NMOP Formulary -None

C. Clarifications to the NMOP Formulary - None

3. **QUANTITY LIMIT CHANGES (NMOP AND RETAIL NETWORK)**

A. Quantity limit for Pegfilgrastim Injection (Neulasta; Amgen): 2 syringes per 45-day supply (NMOP); 1 syringe per 21-day supply (retail network).

4. **CHANGES TO THE PRIOR AUTHORIZATION PROGRAM (NMOP AND RETAIL NETWORK)** - None

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MCCS-GPE **7 May 2002**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Executive Council Meeting

1. The DoD P&T Executive Council met from 0800 to 1600 hours on 7 May 2002 and from 0800 to 0815 hours on 8 May 2002 at the Officers Club, Fort Sam Houston, TX.

2. MEMBERS PRESENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
LTC (P) Joel Schmidt, MC	Army
MAJ Brett Kelly, MS	Army
COL John R. Downs, MC	Air Force
COL Mark Nadeau, MC (Representing COL Bill Sykora, MC)	Air Force
LtCol George Jones, BSC	Air Force
CAPT (select) Matt Nutaitis, MC	Navy
CDR Kevin Cook, MSC	Navy
CAPT Robert Rist	Coast Guard
Dick Rooney	Department of Veterans Affairs
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
LTC Mike Kieffer, MS	Joint Readiness Clinical Advisory Board

MEMBERS ABSENT

COL Rosa Stith, MC	Army

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
CAPT Betsy Nolan, MSC	Navy Pharmacy Specialty Leader
COL Mike Heath, MS	Army Pharmacy Consultant; Chair, DoD Pharmacy Board of Directors
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
LtCol Ed Zastawny, BSC	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC	DoD Pharmacoeconomic Center
LTC Don De Groff, MS	DoD Pharmacoeconomic Center
LTC (P) Doreen Lounsbery, MC	DoD Pharmacoeconomic Center
LCDR Ted Briski, MSC	DoD Pharmacoeconomic Center
SFC Agustin Serrano	DoD Pharmacoeconomic Center
HM1 Lisa Drumm	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
Dave Bretzke	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
Paul Vasquez	Defense Supply Center Philadelphia
CAPT Howard Hays, MD	USPHS/Indian Health Service
CAPT Samuel Hope	USPHS/Indian Health Service
CAPT Robert Pittman	USPHS/Indian Health Service
LCDR Thomas Berry	USPHS/Indian Health Service

3. REVIEW MINUTES OF LAST MEETING

The minutes from the last meeting were accepted as written.

4. INTERIM DECISIONS/ADMINISTRATIVE ISSUES

Four members of the Indian Health Service (IHS) National Formulary Work Group attended the DoD P&T Executive Council meeting. The IHS is evaluating the feasibility of establishing a national formulary.

5. LEVONORGESTREL 0.75 MG (PLAN B)

At the February 2002 DoD Pharmacy & Therapeutics (P&T) Executive Council meeting, the Council recommended the addition of levonorgestrel 0.75 mg (Plan B) to the Basic Core Formulary (BCF), subject to the review and approval of the Director, TRICARE Management Activity (TMA) and/or the Assistant Secretary of Defense for Health Affairs (ASD (HA)). On 28 March 2002, the Executive Director of TMA signed an Action Memo approving the recommendation. On 3 April 2002 the co-chair of the DoD P&T Committee informed the Council members and service pharmacy consultants of the decision, and re-informed the Council on 7 May 2002. On 8 May 2002 the Executive Council was reconvened briefly to announce that the Council co-chairs had been informed that the ASD (HA) also wanted to review the Council's recommendation and that the Executive Director of TMA had rescinded his earlier approval. Therefore, Plan B has NOT been approved for addition to the BCF at this time, and the ASD (HA) is reviewing the Council's recommendation.

MTFs are required to include all BCF drugs on their local formularies. As a result of Plan B's removal from the BCF, each MTF's P&T committee must now re-evaluate whether this product is within the scope of practice at the MTF and whether the MTF wants to continue to have Plan B on its formulary.

6. NATIONAL PHARMACEUTICAL CONTRACTS AND BLANKET PURCHASE AGREEMENTS (BPAs)

Contract awards, renewals, and terminations

- Contracts for oral contraceptives, etodolac, fexofenadine, hydrochlorothiazide, insulin needle/syringes, isosorbide mononitrate, capsaicin cream, and ticlopidine were renewed.
- New contracts were awarded for ibuprofen tablets and fluoxetine capsules.
- DoD contracts for lisinopril and hepatitis A are up for renewal.
- The following joint DoD/VA contracts are up for renewal: ointment base, carbidopa/levodopa SA; glyburide tablets, amantadine capsules, fluocinonide cream/ointment, terazosin tablets/capsules, sotalol tablets, bupropion tablets, acyclovir tablets/capsules, hydroxyurea capsules, pentoxifylline tablets, rifampin capsules, and sucralfate tablets.
- The following joint DoD/VA contracts are up for resolicitation: salsalate tablets, prednisone tablets, and cimetidine tablets.
- The following joint DoD/VA contracts are in various stages of solicitation: benztropine mesylate tablets, minoxidil tablets, carbidopa/levodopa IR tablets, famotidine, chlorpromazine tablets, thiothixene, penicillin VK tablets, dicloxacillin capsules, cephalexin capsules, amoxicillin capsules, and trihexyphenidyl.

7. REEVALUATION OF THE BASIC CORE FORMULARY (BCF)

A. BCF Objective – As outlined in HA Policy 98-034, the objective of the BCF is to ensure the uniform availability of cost-effective pharmaceuticals at MTF pharmacies in order to meet the majority of patients' primary care needs. An analysis of prescriptions dispensed by MTF pharmacies between 1 Oct 01 and 15 Mar 02 revealed that 62% were for BCF items if prescriptions for OTCs were included, and 71% if OTC items were excluded. These data suggest that the BCF objective is being accomplished to a substantial degree.

Some people propose that a large number of drugs should be added to the BCF in order to retain and recapture prescription workload from retail pharmacies where the drugs cost more. This proposal assumes that the addition of a drug to the BCF will actually cause patients to get their prescriptions filled at an MTF rather than a retail pharmacy. Many factors influence patient behavior, so it is difficult to predict the impact that BCF status will actually have on the retention/recapture of prescription workload.

The Council faces a dilemma: Should inclusion on the BCF be reserved for only the more cost-effective drugs in an attempt to encourage the use of agents that offer the best overall value? Or should the Council simply ignore the BCF objective and add a bunch of drugs to the BCF (regardless of their cost-effectiveness) in the hope that it will help retain

and recapture workload from retail pharmacies? The Council did not reach a consensus on this issue.

B. OTC Coverage on the BCF – TRICARE policy provides limited coverage of OTC drugs at retail pharmacies and the NMOP. Chapter 7, Section 7.1 of the TRICARE Policy Manual states that: "Insulin and related supplies may be cost-shared for diabetic patients, regardless of whether or not a prescription is required under state law"; and "Vitamins may be cost-shared only when used as a specific treatment of a medical condition." Non-covered benefits include: "Drugs, including compounded preparations, that are available over the counter."

Although TRICARE policy does not govern the availability of OTC products at MTF pharmacies, the Council has historically refrained from adding OTC products to the BCF. The BCF currently includes only 11 OTC items. The recently published Uniform Formulary Proposed Rule states, "The Basic Core Formulary (BCF) is a subset of the Uniform Formulary and is a mandatory component of all MTF pharmacy formularies". If the BCF is to be a subset of the Uniform Formulary, the inclusion of OTCs on the BCF will be limited by TRICARE policy.

From 1 Oct 01 to 15 Mar 02, MTFs dispensed 3.7 million prescriptions for OTC drugs, which accounted for 16.3% of total prescriptions dispensed during that time period. The eleven OTC items on the BCF accounted for only 500,000 of the 3.7 million prescriptions for OTC drugs, so MTFs clearly provide many more OTC drugs than those included on the BCF.

In light of the Uniform Formulary Proposed Rule, the Council unanimously voted not to add any additional OTC products to the BCF beyond those identified in the TRICARE Policy Manual. However, the Council encourages MTFs to continue providing OTC medications when they represent cost-effective alternatives to legend drugs. The Council will explore mechanisms other than the BCF to promote uniform availability of cost-effective OTC medication at MTFs.

C. Comparison of the BCF to VA's National Formulary - The term "formulary" most properly refers not only to a list of drugs on the formulary of a health care institution or system, but also to related information concerning the use of drugs and to the drug use policies of that institution or system as a whole. The BCF and the VA National Formulary (NF) have fundamental differences that reflect underlying differences in the MHS and VA drug delivery systems, despite similar underlying concepts—both are intended to make cost-effective drug therapies uniformly available across large health care systems. Formulary status on the BCF and/or the NF is increasingly being used to leverage lower prices for commonly used pharmaceuticals in classes where several therapeutically equivalent alternatives exist.

One of the fundamental differences between DoD and the VA that affects formulary structure is the fact that VA facilities generally do not fill prescriptions from outside providers. The VA also lacks a full-service mail order point of service analogous to the NMOP (the VA Consolidated Mail Outpatient Pharmacy (CMOP) is used to expedite the processing of refills) and VA beneficiaries do not have the option of taking their prescriptions to retail network pharmacies. In addition to point of service and

administrative differences, there are well-known patient population differences between the two systems that may affect drug formularies.

DoD and the VA differ even when considering only MTFs and VA facilities, most notably in the degree to which local formulary decision-making is retained by individual facilities. In the VA, the NF is supplemented by 22 regional (VISN) formularies, but local formularies are forbidden and local formulary decision-making is restricted to antimicrobials (to accommodate local resistance patterns). The BCF is supplemented by both regional (in some cases) and local formularies; individual facilities typically have independent P&T committees that retain broad autonomy over local formularies and drug use policy.

The NF drug list contains 1214 items (individual listings) in 28 categories, while the BCF contains 176 items in 24 categories. These counts were based on using the VA classification system and the formularies as listed on the VA PBM and DoD PEC websites as of May 02, after adjusting both lists to use common terminology. The VA drug classification system was chosen for this comparison because it provides consistent categories for all items on both the NF and the BCF, including medical supply items.

Three major categories where the two formularies differ substantially are injectable medications, medical supply items, and OTC medications. The NF contains a large number of medications that have not been traditionally represented on the BCF, including 344 injectable medications, most of which are typically only used on an inpatient basis (compared to 7 on the BCF); 131 medical supply items, including syringes, dressings, IV supplies, catheters, etc. (compared to 2 on the BCF); and 185 OTC medications (vs. 11 on the BCF).

Even if injectable medications, medical supply items, and OTC medications are excluded, the NF still contains more line items than the BCF (570 vs.156). The difference can be broken down into three primary contributing factors:

1) The NF contains some categories, such as antimicrobials, central nervous system medications (including antidepressants and antipsychotics), and antineoplastics, which appear to contain virtually all commonly used drugs in those categories. This may be due to resistance concerns (as would be the case with antimicrobials) or to lack of therapeutic interchangeability of drugs in these categories. Some of these drugs may be subject to criteria for use.
2) The NF covers some types of drugs traditionally not well represented on the BCF because they are considered to be specialty drugs (e.g., antineoplastics, antivirals, diagnostic agents, topical anesthetics).
3) The NF tends to list more alternatives than the BCF even in commonly used drug classes listed on both formulary lists. For example, the NF lists 5 oral glucocorticoids while the BCF lists 2, and the NF lists 8 nonsteroidal anti-inflammatory drugs while the BCF lists 3.

8. DRUG USE AND EXPENDITURE REVIEW

The Council was unable to assess the FY 02 budget execution by MTF pharmacies because:

- Prime vendor data are missing for so many MTFs that expenditures cannot be accurately estimated.
- CHCS pharmacy cost reports are not uniformly available from MTF pharmacies.
- MTF pharmacy expenditures reported by the TMA resource management differ significantly from the pharmacy expenditures reported by the resource managers for the three services.

9. PENDING CONTRACT INITIATIVES

A. Status of Contracting Initiative for Leutinizing Hormone Releasing Hormone (LHRH) Agonists – The DoD and the VA have agreed in principle on pursuing a contract for a Leutinizing Hormone Releasing Hormone (LHRH) agonist. The solicitation will be for a 1 and 3 month product from the same manufacturer for the treatment of prostate cancer; other formulations and strengths will not be included. The solicitation is currently being written, but has not yet been released.

B. Status of Contracting Initiative for Nasal Corticosteroids – The DoD and VA issued a joint solicitation to select a single source for flunisolide nasal inhalers. This solicitation does not stipulate that the contracted drug will be on the BCF. The DoD and VA are also working on a joint solicitation for a once-daily nasal corticosteroid inhaler that will place the contracted product on the BCF.

C. Status of Contracting Initiative for Triptans – The DoD and VA are working on a joint solicitation that will comply with the Council's previous stipulation that any contracting initiative must either allow or require MTFs to have at least two triptans on their formularies.

10. DRUG CLASS EVALUATIONS TO DETERMINE CLINICALLY ACCEPTABLE CONTRACTING/FORMULARY STRATEGIES

: COL Remund briefed the Council on the PEC's attempt to outline the process that the Council has been using to identify clinically acceptable contracting/formulary strategies for drug classes. The Council followed the process described in Appendix A to evaluate the following drug classes.

A. Statins – The current DoD statin contract will expire in February 2003. A joint solicitation with the VA for a follow-on contract is currently being considered. A high potency statin (simvastatin or atorvastatin) must be included on the BCF in order for patients to attain the LDL-cholesterol goals established by the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III guideline. A low potency statin could also be included on the BCF if it would enhance the cost effectiveness of cholesterol-lowering therapy in the Military Health System. The following analysis focuses on the high potency statins.

Therapeutic Interchangeability: Although atorvastatin can achieve larger reductions in LDL-cholesterol than simvastatin, less than 10% of patients require the magnitude of LDL-cholesterol reduction that can only be achieved by atorvastatin. Some studies indicate that atorvastatin may not raise HDL cholesterol levels as much as simvastatin, but the Council doubted that any difference in the effect on HDL levels would significantly affect the therapeutic interchangeability of these drugs for most patients. Long-term clinical trials prove that simvastatin reduces cardiovascular morbidity and mortality. Similar evidence is not available for atorvastatin. There are no data that demonstrate significant differences in safety or tolerability between atorvastatin and simvastatin. The Council concluded that simvastatin and atorvastatin have a high degree of therapeutic interchangeability.

Clinical Coverage: Simvastatin and atorvastatin each have the capacity to satisfy the LDL-cholesterol reduction needs of at least 90% of the DoD population. Some patients may have a clinical need to use pravastatin because of its lower potential for drug interactions, but these patients comprise less than 5% of statin patients. Providers expressed a preference for having more than one statin on the BCF, but they did not provide a clinical justification for a second statin on the BCF. The Council concluded that either atorvastatin or simvastatin would provide adequate clinical coverage.

Provider Acceptance: Provider acceptance of simvastatin is clearly supported by the fact that simvastatin currently accounts for about 95% of all statin prescription fills at MTF pharmacies. Providers also expressed a willingness to use atorvastatin. Providers voiced strong opposition to any contract that would require patients to be switched from one statin to another statin. Opposition to switching patients is understandable because (1) approximately 150,000 patients had to switch statins after the DoD statin contracts were awarded in August 1999 and (2) approximately 100,000 patients had to switch statins after cerivastatin was withdrawn from the market in August 2001.

The Council voted unanimously to support any contracting/formulary strategy (to include a closed class contract) that places at least one high potency statin on the BCF and does not require patients to be switched from one agent to another. The Council also supports the inclusion of a low-potency statin on the BCF if it is projected to enhance the cost-efficiency of statin therapy.

B. Angiotensin Receptor Blockers (ARBs) –Seven ARBs are available: losartan (Cozaar, FDA-approved in Apr 95), valsartan (Diovan, Dec 96), irbesartan (Avapro, Sep 97), candesartan (Atacand, Jun 98), telmisartan (Micardis, Oct 98), eprosartan (Teveten, Oct 99), and olmesartan (Benicar, Apr 02). All the ARBs are FDA-approved for hypertension.

ARBs offer a slight clinical advantage (lower incidence of cough and angioedema) compared to angiotensin-converting enzyme inhibitors (ACEIs) in the treatment of hypertension, but ARBs cost much more than ACEIs. The JNC-VI Guideline advises that ARBs should be reserved for hypertensive patients who are unable to tolerate ACEIs. ARBs are also used “off-label” for congestive heart failure (CHF) and prevention of renal disease progression in diabetics. Despite a recent ADA recommendation that an ARB should be used as first line therapy in type 2 diabetes with hypertension and

microalbuminuria or clinical albuminuria, many providers still think that ARBs should be reserved for second line therapy when patients experience adverse effects on an ACEI.

Despite their "second line" place in therapy, ARB purchases by MTFs increased about 56% from $9 million in FY 00 to $14 million in FY 01. A significant price reduction might be achieved through a contracting initiative that places one or more ARBs on the BCF.

Therapeutic Interchangeability

- *Hypertension*: The Council considered the information contained in a joint VA/DoD clinical review of the ARBs (published on the PEC website). The Council concluded that ARBs have a high degree of therapeutic interchangeability in the treatment of hypertension.
- *CHF*: The FDA has characterized valsartan as "approvable" for CHF in patients not receiving an ACEI or as a substitute for an ACEI (despite the FDA advisory committee recommendation against approval). The ELITE I study showed increased survival for CHF patients on losartan compared to an ACEI, but the larger ELITE II study showed no significant difference in all-cause mortality for patients on losartan compared to an ACEI. The RESOLVD trial was discontinued because candesartan was associated with an increase in hospitalizations and death compared to CHF patients treated with enalapril. A large CHF trial comparing candesartan to an ACEI (the CHARM trial) is underway. Data are not available for the other ARBs in the treatment of CHF. The Council decided that the data are insufficient to conclude that the ARBs are therapeutically interchangeable for CHF.
- *Prevention of renal disease progression in diabetics*: A FDA advisory committee concluded that the IDNT and IRMA-2 trials were suggestive of efficacy, but the data were insufficient to support approval of irbesartan for prevention of renal disease progression in patients with type 2 diabetes. An FDA advisory committee recommended approval of losartan for the prevention of renal disease progression in diabetics based on the RENAAL trial. Data are not available for the other ARBs for this indication. The Council decided that the data are insufficient to conclude that the ARBs are therapeutically interchangeable for prevention of renal disease progression in diabetics.

Clinical Coverage: There is no evidence that if a hypertensive patient fails therapy with one ARB, a better response would occur with another ARB. Any of the ARBs would probably provide adequate clinical coverage when used for hypertension, but there are no data to support a conclusion that one or more of the ARBs is sufficiently safe, tolerable, and effective to satisfy the clinical needs of at least 90% of the patients when used for CHF or prevention of renal disease progression in diabetics.

Provider Acceptance: Losartan, valsartan, and irbesartan account for about 90% of prescription fills for ARBs at MTF pharmacies, and providers expressed a preference for these three ARBs. Nephrologists and endocrinologists prefer irbesartan and losartan. Cardiologists prefer valsartan. These three have been on the market longer than the other ARBs, so providers have more confidence in their safety profiles. Providers were uniformly opposed to switching patients from one ARB to another.

The Council unanimously voted to add at least one ARB to the BCF in an open class, with guidelines for appropriate use. The Council also stipulated that any contract for an ARB should not require patients to be switched from one ARB to another ARB.

C. *Thiazolidinediones (TZDs, "glitazones")* – While the TZDs offer a relatively modest reduction in HbA1C compared to other antidiabetics, diabetic patients frequently require combination therapy with two or more agents. Even small reductions in HbA1C correlate with a decreased risk of microvascular complications. There has now been sufficient clinical experience with TZDs to lessen the concern regarding hepatoxicity. The VA is currently considering adding a TZD to its National Formulary. A DoD and VA joint procurement strategy for TZDs might achieve a substantial price reduction.

Therapeutic Interchangeability: There are no large, randomized, controlled head-to-head trials comparing rosiglitazone (Avandia) and pioglitazone (Actos). However, comparison of clinical trial data suggests that they reduce HbA1C by the same degree when equivalent doses are used (pioglitazone 45 mg qd = rosiglitazone 4 mg bid, or pioglitazone 30 mg qd = rosiglitazone 8 mg qd). Both drugs are approved for monotherapy and for use in combination with metformin or a sulfonylurea. Pioglitazone is approved for use with insulin, and the FDA has classified rosiglitazone as "approvable" for use with insulin. There are case reports of heart failure occurring with both drugs when used in combination with insulin. There is insufficient evidence to conclude that the drugs differ in their propensity to cause or exacerbate heart failure.

Comparison of data from clinical trials suggests that pioglitazone has a more favorable effect on LDL-cholesterol and triglycerides than rosiglitazone. However, due to the significant intra-person and inter-person variability in lipid levels, the variability in methods used to measure lipid levels, and potential differences in study subjects across the trials, it is difficult to draw a definitive conclusion about any true differences in lipid effects. The clinical significance of the potential differences in lipid effects is also unknown. Table 1 shows the range of changes in mean lipid levels from clinical trials for rosiglitazone and pioglitazone.

Table 1: Range of Mean Lipid Changes from TZD Clinical Trials

	Rosiglitazone[a]	Pioglitazone[b]
LDL	↑ 5.3 – 22%	↑ 2.8 – 7.7%
HDL	↑ 8.4 – 18%	↑ 9.1– 15.8%
Triglycerides	↑9 – 19.6%	↓ 9.6 – 15.9%

[a] Rosiglitazone LDL results from 7 studies, HDL results from 5 studies, and triglyceride results from 2 studies.
[b] Pioglitazone results from 5 studies.

Rosiglitazone and pioglitazone appear similar to placebo in their propensity to cause elevation in liver transaminases. There are no data to suggest that they differ significantly in their potential to cause hepatotoxicity, edema or weight gain.

Clinical Coverage: Based on their FDA-approved indications, either of these drugs can be expected to have the desired clinical effect in over 90% of patients.

Provider Acceptance: Providers would generally accept either agent, but some indicate a preference for pioglitazone due to its more favorable lipid profile. PDTS prescription data

show that pioglitazone has consistently increased its share of prescription fills for TZDs across all three outpatient pharmacy points of service over the past year.

Council members had difficulty reaching consensus on whether this class is suitable for a closed class contract. Objections to a closed class contract centered on the potential lack of therapeutic interchangeability between pioglitazone and rosiglitazone in regard to their effects on LDL-cholesterol and triglycerides. Some Council members also expressed concern that the potential for discovery of new clinical information about these drugs makes a closed class contract risky for this drug class. After two motions failed, the Council approved a third motion to add one TZD to the BCF via a procurement initiative that leaves the TZD class open and does not require patients to be switched from one TZD to another.

11. DRUG/DRUG CLASS EVALUATIONS TO DETERMINE BCF ADDITION

A. COX-2 Selective Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) – The major advantage of COX-2 selective NSAIDs ("COX-2 inhibitors") compared to non-specific NSAIDs is a reduced incidence of complicated upper gastrointestinal (GI) events (GI bleed, perforation, and obstruction) and symptomatic but uncomplicated ulcers. Evidence that COX-2 inhibitors actually provide this benefit is primarily derived from two large trials: the Vioxx Gastrointestinal Outcomes Research Study (VIGOR) and the Celecoxib Long-term Arthritis Safety Study (CLASS).

VIGOR demonstrated a statistically significant reduction in the annualized incidence of complicated upper GI events in patients receiving rofecoxib (0.6%) vs. naproxen (1.4%), which equates to a number-needed-to-treat (NNT) of 125. In other words, 125 patients would need to be treated with rofecoxib rather than naproxen for one year to prevent one complicated upper GI event. CLASS (celecoxib vs. ibuprofen and diclofenac) failed to demonstrate a statistically significant reduction in complicated upper GI events for its overall patient population, but a statistically significant reduction in complicated upper GI events did occur in the subgroup of patients not receiving aspirin. A statistically significant reduction also occurred for the broader endpoint of complicated upper GI events plus symptomatic but uncomplicated ulcers regardless of aspirin use.

If the reduction in complicated upper GI events in VIGOR is generalized to all COX-2 inhibitors and the daily cost of COX-2 inhibitor and nonspecific NSAID therapy is estimated to be $1.50 and $0.15, respectively, treating 125 patients for one year with COX-2 inhibitors rather than nonspecific NSAIDs would prevent one complicated GI event at an incremental drug cost of about $61,600. This does not take into account the effect of reductions in the incidence of symptomatic but uncomplicated ulcers and possibly in the incidence of GI symptoms and the use of medications to treat GI symptoms (e.g., H2-blockers and PPIs).

Because the risk of NSAID-associated GI events is known to differ among patient populations (based on factors such as age, use of other medications that increase GI risk, use of prophylactic medications, and history of peptic ulcer disease and/or prior GI events), the NNT from the VIGOR trial and the associated cost to prevent one GI event cannot be generalized to all patients. The NNT and the associated costs would be much higher in a patient population without known risk factors (e.g., young patients, many of

whom would receive relatively short-term treatment with NSAIDs) than in the patient population studied in VIGOR (older RA patients requiring chronic NSAID therapy).

Estimates of the background risk of GI events in a general patient population are not readily available. However, if the baseline annualized risk of NSAID-associated GI events in such a patient population is assumed to be about 0.5%, and the relative reduction in events with COX-2 inhibitors vs. nonspecific NSAIDs is assumed to be similar to the reduction in VIGOR (about 50%), the NNT would be 400. Using the same daily medication costs described above, 400 patients would have to be treated for one year with COX-2 inhibitors rather than nonspecific NSAIDs to prevent one complicated GI event, at an incremental drug cost of $197,000.

COX-2 inhibitors appear to be somewhat better tolerated with regard to dyspepsia and other GI symptoms than the non-specific NSAIDs to which they have been compared. COX-2 inhibitors appear similar to non-specific NSAIDs in regard to other adverse effects (e.g., renal adverse effects and propensity to cause edema and blood pressure elevation). COX-2 inhibitors do not affect platelet aggregation.

The VIGOR trial demonstrated a statistically significant increased risk in serious cardiovascular (CV) thrombotic events (primarily acute myocardial infarctions) in patients treated with rofecoxib compared to patients treated with naproxen (1.1% vs. 0.5%). The cause of this finding, its potential applicability to other COX-2 inhibitors, and its real meaning in day-to-day clinical practice are subject to considerable debate. Subsequent analyses of pooled data comparing rofecoxib to NSAIDs other than naproxen or to placebo have not shown an increased in CV risk for rofecoxib.

COX-2 inhibitors do NOT appear to be any more effective than non-specific NSAIDs in the treatment of osteoarthritis, rheumatoid arthritis, acute pain, or dysmenorrhea.

After reviewing the clinical data, the Council reiterated its conclusion that even if COX-2 inhibitors are used only in patients at increased risk for NSAID-associated GI events, the DoD would incur a large increase in drug costs for a rather small decrease in GI events. If COX-2 inhibitors are used in patients with a “normal” risk for GI events, the DoD would incur huge incremental costs for miniscule incremental benefits. The Council acknowledged that the COX-2 inhibitors are being considered for addition to the BCF because of the potential financial impact of shifting prescriptions from the retail network to MTFs—not because of the clinical value they offer in comparison to their cost.

To estimate the potential for increased use of COX-2 inhibitors if a COX-2 inhibitor were added to the BCF, the PEC compared COX-2 inhibitor prescription fill rates (as a percent of all Rx fills) at MTFs that have one or more COX-2 inhibitors on formulary to MTFs that do not have a COX-2 inhibitor on formulary. Assuming that the prescription fill rates at sites that do not currently have a COX-2 inhibitor on formulary would increase to the same rate as sites that do, the total number of COX-2 Rx fills at MTFs would increase by 180,000 per year (32.8%) if a COX-2 inhibitor were added to the BCF. This increase would inevitably include use of COX-2s in both patients likely to benefit (i.e., long-term use in patients with risk factors for GI complications) and patients unlikely to benefit (short-term use in patients without risk factors) from using COX-2 inhibitors.

At the last meeting, the Council asked DSCP to issue a request for Blanket Purchase Agreement (BPA) price quotes to the pharmaceutical companies that market COX-2 inhibitors for the purpose of adding a COX-2 inhibitor to the BCF in an open class. The request for BPA price quotes also asked companies to submit their plans for assisting MTFs in targeting the use of COX-2 inhibitors to the patients at greatest risk for GI events. The VA decided not to participate in this BPA request for quotes.

The Council evaluated the projected weighted average daily cost per patient that would result from the price quotes offered for each COX-2 inhibitor. The Council also used a mathematical model to estimate the potential financial impact of adding each COX-2 inhibitor to the BCF. The model took into account likely increases in use and projected shifts in utilization amongst the three points of service. After evaluating a variety of scenarios, the Council concluded that it was in the best interest of the government not to accept any of the BPA price quotes, so a COX-2 inhibitor was not added to the BCF.

B. Raloxifene (Evista) – Raloxifene was evaluated for potential addition to the BCF based on high retail network use. PDTS data from July through December 2001 showed 37,200 prescriptions for 13,000 unique patients in the retail network, with an annual cost to DoD of $5 million.

Raloxifene is the first of a new class of agents known as selective estrogen receptor modifiers (SERMs). A derivative of tamoxifen, raloxifene has a mixed agonist-antagonist effect on estrogen receptors throughout the body. It is indicated for the prevention and treatment of osteoporosis in postmenopausal women. Alendronate, also approved for the treatment of osteoporosis, is currently on the BCF.

The most common side effects of raloxifene are hot flashes and leg cramps. Patients treated with raloxifene were at higher risk of venous thromboembolism (NNH 143) than the placebo group. The increased risk is similar to the risk of venous thromboembolism seen with hormone replacement therapy (HRT). In the MORE trial, raloxifene reduced the risk for new vertebral fractures by 50% in women without previous fractures (NNT 46) and by 30% in those with previous fractures (NNT16). Both reductions were statistically significant. Raloxifene also increased BMD of the femoral neck and spine by 2-3%. The drug cost to prevent one vertebral fracture in 3 years is $42,000 compared to a cost of $27,000 for alendronate to prevent one vertebral fracture in 3 years.

Raloxifene's nonskeletal effects include reductions in LDL cholesterol (11%) and total cholesterol (7%), without changes in HDL cholesterol. Raloxifene reduced the risk of invasive breast cancer by 76% in the MORE trial. Studies are underway to investigate the cardiovascular benefits of raloxifene and to compare it to tamoxifen in the prevention of breast cancer.

Providers and pharmacists were surveyed regarding their use and potential use of raloxifene. Eighty-five responses were obtained. All responses favored the addition of raloxifene to the BCF. Raloxifene 60 mg is currently on the formulary of approximately 20% of MTFs.

The Council voted to add raloxifene to the BCF.

C. *Calcium (calcium and calcium + vitamin D)* – Given the Council's previous decision not to add any OTC medications to the BCF beyond those identified in the TRICARE Policy Manual, the Council did not consider the proposal to add calcium and calcium + vitamin D to the BCF. The Council acknowledged that clinical data fully support the use of calcium in patients with osteoporosis and especially in patients treated for osteoporosis with prescription medications. The Council encourages all MTFs to make available and promote adequate calcium supplementation in patients for the prevention and treatment of osteoporosis.

D. *Guaifenesin/pseudoephedrine sustained release tablet (generic Entex-PSE)* – Entex-LA eq. (guaifenesin & phenylpropanolamine long-acting) was removed from the BCF at the Nov 00 P&T Committee meeting because of safety concerns expressed by the FDA regarding phenylpropanolamine. The Committee had intended to select an alternative agent for the BCF after manufacturers reformulated their products, but an alternative agent was not selected. The PEC recently identified that guaifenesin (GFN) and pseudoephedrine (PSE) long-acting, the logical replacement for Entex-LA eq., was the second most prescribed non-BCF drug. Many different brands and formulations exist (e.g., Entex-PSE, Duratuss, Deconsal-II), but MTFs overwhelmingly use the GFN 600mg/PSE 120mg formulation. Three manufacturers currently offer prices of less than $0.07 per tablet for this product. The Council unanimously voted to add GFN 600 mg/PSE 120 mg long acting to the BCF.

12. CLARIFICATION OF BCF LISTING

Carbinoxamine/pseudoephedrine (Rondec) Drops — Lt Col Zastawny presented a clarification of the BCF listing of carbinoxamine/pseudoephedrine drops. A recent formulation change for the branded product (Rondec®) decreased the concentrations of the ingredients from 2mg carbinoxamine and 25mg of pseudoephedrine per mL to 1mg carbinoxamine and 15 mg of pseudoephedrine per mL. Changes were also made in the recommended dosing schedule included with the product. The new 1mg/15mg per mL formulation appears to be the only formulation currently being produced by the brand and generic manufacturers. The change in recommended dosing raises concern about the potential for dosing errors resulting in excessive dosing of pseudoephedrine in pediatric patients if the two dosage forms were used interchangeably.

The Council agreed to (1) specify the newer carbinoxamine 1mg and pseudoephedrine 15mg per mL formulation on the BCF, 2) remove the Rondec® brand name reference from carbinoxamine/pseudoephedrine drops listing on the BCF, and 3) provide a link from the BCF listing to a drug and dosing information page.

13. MTF REQUESTS FOR BCF CHANGES

A. *Request to remove propranolol LA from the BCF* – A request to delete propranolol long-acting (LA) from the BCF cited lack of generic availability and low utilization. The PEC confirmed the shrinking availability of generic forms of propranolol LA. Approximately 4000 patients use propranolol LA. The number of unique users has remained relatively constant over the past three years. The Council voted to delete propranolol LA from the BCF because of decreasing generic availability and availability of preferable alternatives on the BCF (e.g., metoprolol, atenolol).

B. Request to add Combivent (18 mcg ipratropium/103 mcg albuterol) MDI to the BCF – An Air Force pulmonologist provided the following rationale for the request:

- Seven studies have shown that the addition of an anticholinergic with a beta agonist can achieve enhance bronchodilation.
- Patients with COPD (stage II and III) are required to take both medications. Combivent is included as the standard of care in the VHA/DoD, ATS, and new GOLD guidelines for the management of COPD.
- Compliance with a MDI increases when only one device or inhaler is used and guarantees the patient receives both medications for maximal effect.

Safety and tolerability of the combination product are similar to the same dosages of the products administered by separate inhalers. Combination therapy with ipratropium and albuterol has been shown to produce superior bronchodilation without additional side effects compared to monotherapy with albuterol or ipratropium. In stage II and III COPD, a combination of ipratropium plus a beta-agonist is associated with lower rate of exacerbations and lower total health-care costs than compared to albuterol or ipratropium monotherapy. Efficacy of Combivent is similar to the same dosages of the ipratropium and albuterol administered by separate inhalers.

The PEC requested provider (physician and pharmacist) input on this issue and received 33 responses: 26 favoring, 5 against, and 2 inconclusive regarding addition of Combivent to the BCF. Providers made several key points:

- This medication is used in patients with COPD, who frequently are noncompliant and smoke. They need the ipratropium to assist with lung function, but they don't necessarily feel the effect like they do with albuterol.
- Each inhaler requires 2 inhaled puffs 3-5 minutes apart, and to do both albuterol and ipratropium at a time would take up to 20 minutes, which most patients are not willing to do. Combivent only takes 3-5 minutes, and they won't get the two confused.
- The addition of Combivent to the BCF may improve patient satisfaction and compliance.
- Although we see a fair amount of civilian prescriptions, it is not on our MTF formulary. If it is cheaper for us to fill than the Tricare network, than I guess that would be a positive.
- There is a potential to reduce waste and pharmacy labeling costs from the use of two products.

Prime vendor data show that nonavailability of the contracted brand of albuterol MDI causes MTFs to actually pay more than the contract price for albuterol MDIs. FSS and contract pricing as of April 02 for Combivent and the individual products compared to the MTF average price paid (Nov 01- Jan 02) are presented in the following table:

Item Description	Doses/container	FSS Price As of April 02	MTF Ave Price (PV data Nov 01 – Jan 02)
Albuterol MDI	200	$ 1.65 (Contract price as of Nov 01)	$ 3.26
Ipratropium MDI	200	$ 19.59	$ 18.82
Combivent MDI	200	$ 22.47	$ 21.59

The cost of Combivent is compared to the cost of the individual products using both lowest available FSS price and MTF average price in the following table:

	Combivent cost/day 2 puffs four times daily	Cost/day of equivalent dose of individual products	Additional cost per day for Combivent
FSS Price	$ 0.90	$ 0.85	$ 0.05
MTF Ave Price	$ 0.86	$ 0.88	($ 0.02)

Combivent is on approximately 53% of MTF formularies. It ranks #25 in total MTF prescription fills of legend drugs that are not currently on the BCF. Combivent also falls in the top 100 prescriptions filled in the retail network.

Addition of Combivent to the BCF could improve patient satisfaction and compliance. There is also a potential reduction in waste. There is a potential for cost savings to the government since the average MTF price for Combivent is $0.02/day less expensive than the cost/day of equivalent dose of individual products. The Council voted to add ipratropium/albuterol (Combivent) to the BCF.

C. *Request to remove Fosamax 5 and 10 mg from the BCF* – The PEC received a request to remove the 5 mg and 10 mg strengths of alendronate, citing low usage of the daily dosage forms of these agents since the weekly forms became available. In general, the BCF listing of a drug includes all formulations and dosage strengths. The Council found no compelling reason to change the listing for alendronate, and voted unanimously to retain alendronate 5 mg and 10 mg on the BCF. Individual MTFs must make the drug available, in all strengths, when needed. Decisions about stocking levels may be made at the MTF level based on usage at that facility.

14. ADJOURNMENT

The meeting adjourned at 1600 hours on 7 May 2002. The next meeting will be held at the Uniformed Services University of the Health Sciences, Bethesda, Maryland at 0800 on 7 August 2002. All agenda items should be submitted to the co-chairs no later than 8 July 2002.

<signed>	<signed>
DANIEL D. REMUND	TERRANCE EGLAND
COL, MS, USA	CDR, MC, USN
Co-chair	Co-chair

Appendix A: Drug Class Evaluations to Determine Clinically Acceptable Contracting/Formulary Strategies

1. The DoD P&T Executive Council evaluates the relative safety, tolerability, efficacy, price/cost and other pertinent issues ("STEPO" evaluation) to assess three factors that affect the acceptability of various contracting/formulary strategies:

   a. *Therapeutic interchangeability*: Therapeutic interchangeability is the extent to which drugs have similar clinical attributes, are used for the same indications, are used for the same patient populations, and can be expected to achieve similar clinical outcomes. Closed class contracts that require patients to be switched to the contracted drug require the highest degree of therapeutic interchangeability.

   b. *Coverage of clinical needs*: The drug(s) selected for a closed class contract must be sufficiently safe, tolerable, and effective to satisfy the clinical needs of at least 90% of the patients for whom the drug will be prescribed. Too many patients and providers will be forced to use the non-formulary/special order process if fewer than 90% of the patients can be successfully treated with the contract drug.

   c. *Provider acceptance*: Provider acceptance is the extent to which DoD providers are willing to use the contracted drugs and refrain from using the non-contracted drugs. There are two components to this condition. The first relates to provider behavior when first starting a patient on one of the agents in the class. For some drug classes providers will not accept a requirement to prescribe a particular agent even though it has been determined to be therapeutically equivalent to other members of the class. This is often true of newly approved drugs, but may apply to other members of the class as well. A lack of long-term safety data is a common cause for this concern. The second component relates to whether prescribers are willing to switch patients currently being treated with one drug in a class to the contract winner following contract award. Willingness to switch is tied to the perceived likelihood that the contracted drug will effectively substitute for the patient's current therapy and the amount of effort it takes to make the switch.

2. The DoD P&T Executive Council then decides which (one or more) of the contracting/formulary strategies described below are clinically acceptable and specifies any "clinical imperatives" that must accompany a given strategy. The VA/DoD Pharmaceutical Contracting Workgroup decides which specific contracting strategy to use from among the strategies that are acceptable to the DoD P&T Executive Council. Potential contracting/formulary strategies include the selection of one or more drugs for:

   a. A closed class contract that puts the contracted drug(s) on the BCF and requires patients to be switched to the contract drug(s).

   b. A closed class contract that puts the contracted drug(s) on the BCF, but does not require existing patients to be switched to the contracted drug(s).

   c. A closed class contract that does not put the contracted drugs(s) on the BCF, but requires existing patients to be switched to the contract drug(s).

   d. A closed class contract that does not put the contracted drugs(s) on the BCF and does not require existing patients to be switched to the contract drugs.

   e. A contract that puts the contracted drug(s) on the BCF but leaves the class open.

   f. The BCF based on an evaluation of the responses to a Blanket Purchase Agreement (BPA) request for price quotes

   g. The BCF based on a BPA(s) offered by one or more companies

   h. The BCF based on existing BPA(s)

   i. The BCF based on existing FSS prices

Department of Defense
Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **13 FEBRUARY 2002**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee Meeting

1. A meeting of the DoD P&T committee convened at 0800 hours on 13 February 2002, at the Non-Commissioned Officers Club, Fort Sam Houston, TX

2. MEMBERS PRESENT

CDR Terrance Egland, MC, USN	DoD P& T Committee Co-chair
Col John R. Downs, MC	Air Force
Col Mark Nadeau, MC (For Col Bill Sykora, MC)	Air Force
LtCol (select) George Jones, BSC	Air Force
CAPT (select) Matt Nutaitis, MC	Navy
CDR Kevin Cook, MSC	Navy
MAJ Brett Kelly	Army
LTC (P) Joel Schmidt, MC	Army
CAPT Robert Rist	Coast Guard
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
William Hudson	Humana
Gene Lakey	TriWest
Ron McDonald	Sierra Military Health Services
Trevor Rabie	Uniformed Services Family Health Plans (USFHP)
Dick Rooney	Department of Veterans Affairs

MEMBERS ABSENT

COL Daniel D. Remund, MS, USA	DoD P& T Committee Co-chair
COL Rosa Stith, MC	Army
LTC Mike Kieffer, MS	Joint Readiness Clinical Advisory Board
Ray Nan Berry	Health Net Federal Services

OTHERS PRESENT

COL William Davies, MS, USA	DoD Pharmacy Program Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
CAPT Joe Torkildson, MC, USN	DoD Pharmacoeconomic Center
LCDR Ted Briski, MSC, USN	DoD Pharmacoeconomic Center
LCDR Denise Graham, MSC, USN	DoD Pharmacoeconomic Center
LtCol Ed Zastawny, USAF BSC	DoD Pharmacoeconomic Center
LTC Doreen Lounsbery, MC, USA	DoD Pharmacoeconomic Center
Maj Barb Roach, USAF MC	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
David Bretzke	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
SFC Agustin Serrano	DoD Pharmacoeconomic Center
MAJ Cheryl Filby, MS, USA	Defense Supply Center Philadelphia
CDR Brian Kerr, MSC, USN	Defense Supply Center Philadelphia
Paul Vasquez	Defense Supply Center Philadelphia
Vincent Valinotti	Defense Supply Center Philadelphia
David Chicoine	Uniformed Services Family Health Plan
Mark Petruzzi	Merck-Medco
Elizabeth Scaturro	Merck-Medco Managed Care

3. **REVIEW MINUTES OF LAST MEETING / ADM INISTRATIVE ISSUES** – The minutes from the last meeting were accepted as written.

4. **INTERIM DECISIONS** – No interim decisions.

5. **REPORT FROM THE DOD EXECUTIVE COUNCIL MEETING –** CAPT Torkildson reported on the additions to the BCF:

   - Advair (fluticasone/salmeterol) Inhaler: all strengths
   - Prempro (conjugated estrogen and medroxyprogesterone): all strengths.
   - Zithromax (azithromycin) 250 mg tablets; does not require the Z-pak dosage formulation.

6. **IMPLEMENTATION OF PHARMACY BENEFIT PROVISIONS IN THE FY00 AND FY01 NATIONAL DEFENSE AUTHORIZATION ACTS** - COL Davies will present the proposed rules at the next meeting if the document has been published. COL Davies stated that Managed Care Support Contractors have submitted nominations for providers to the DoD P&T Committee.

7. **PPI UTILIZATION IN THE NMOP** – CAPT Torkildson reported on proton pump inhibitor (PPI) use in all three points of service. There was a substantial decrease in the number of PPI prescriptions filled at MTFs during the Thanksgiving and Christmas holiday seasons, which raises questions regarding access. The total number of prescriptions for PPIs filled in the NMOP remains fairly flat while the retail network is showing a gradual growth rate. An analysis of the market share of the various PPIs by point of service reveals an increase in rabeprazole (Aciphex) use in the MTFs,

while the retail network analysis reveals a growing use of esomeprazole (Nexium) and stable use of omeprazole. The market share of omeprazole in the NMOP remains high at around 75% of all PPI prescriptions, with a slight upward trend in esomeprazole use. An analysis of the average cost per unit for PPIs for each point of service shows that the cost has declined by over 50% in MTFs, has remained flat in the retail network, and increased in the NMOP due to an omeprazole price increase. The Committee took no action on this information, but will continue to monitor the class.

8. **GENERIC LOVASTATIN IN THE NMOP** –The impact of the recent approval of a generic formulation of lovastatin on the current statin contract and the potential for creating patient dissatisfaction regarding the current structure of copays was discussed. The situation has been created in which a patient might submit a prescription for lovastatin to the NMOP in order to obtain the $3.00 generic copay, only to be told that they must use the contracted drug simvastatin and pay a $9.00 copay. COL Davies stated that it is not within the purview of this committee to reduce the co-pay for simvastatin to the generic copay since it did not compete directly against generic products. In a closed class contract, medical necessity is required in order to go outside the contract. When presented with a statin prescription other than simvastatin, the NMOP should call the provider and determine if there is a medical necessity for the noncontracted statin. If not, the contract situation should be explained to the provider, and an opportunity presented to switch to simvastatin. If the provider is not willing to change the prescription, the prescription should be returned to the patient and their options explained to them.

9. **BCF AND NATIONAL MAIL ORDER PHARMACY (NMOP) FORMULARY ISSUES** – The Committee determined the NMOP formulary status, NMOP or retail network formulary restrictions (quantity limits or prior authorization), and Basic Core Formulary (BCF) status for 13 new drugs (see Appendix A).

10. **ANTIBIOTIC PROPHYLAXIS FOR ANTHRAX EXPOSURE** – CAPT Torkildson reported that the utilization of doxycycline and ciprofloxacin at the NMOP and in the retail network has returned to baseline levels. The Committee concluded that there is no further need to report on this subject unless subsequent events create the possibility of change.

11. **PRIOR AUTHORIZATIONS**

A. *Cost avoidance from NMOP prior authorizations (PAs)* – Shana Trice (PEC) reported that, for the 1st quarter of FY 02, the NMOP PAs for sildenafil, COX-2 inhibitors, and etanercept resulted in an estimated cost avoidance per new prescription submitted of $51.91 for sildenafil, $15.64 for COX-2 inhibitors, and $276.74 for etanercept. The estimated cost avoidance per new prescription submitted is based on the cost avoidance model outlined in the Aug 00 DoD P&T Committee minutes. Since these estimates are consistent with previous reports, the Committee did not make any changes to these PAs.

B. *Changes to PA criteria for COX-2 inhibitors* – The Committee addressed two issues: 1) a new FDA-approved indication for celecoxib (Celebrex) for acute pain in adults and treatment of primary dysmenorrhea; and 2) the availability of a new COX-2 inhibitor valdecoxib (Bextra). The FDA approved valdecoxib in Nov 01 for treatment of osteoarthritis (OA), adult rheumatoid arthritis (RA), and primary dysmenorrhea.

Existing NMOP PA criteria for COX-2 inhibitors allow use of rofecoxib but not celecoxib for 20 days or less in patients with risk factors for GI adverse events, since celecoxib previously lacked any indication for acute use. The Committee approved the following revised COX-2 inhibitor criteria for all COX-2 inhibitors (celecoxib, rofecoxib, valdecoxib):

- *Benefit coverage NOT provided for:*
    - *Concurrent anti-inflammatory therapy with any NSAID or aspirin at doses > 325 mg per day, or*
    - *The prevention of colon cancer, or*
    - *The prevention or treatment of Alzheimer's disease*
- *Benefit coverage provided for:*
    - *Patient has previously failed an adequate trial with at least two different NSAIDS,*

      OR
    - *COX-2 therapy AND high risk for NSAID-induced gastropathy OR use of a NSAID could result in destabilization or risk. Identified by an of the following:*
        - *Concurrent oral corticosteroids, anticoagulants, antiplatelet agents*
        - *History of PU*
        - *History of NSAID related ulcer*
        - *History of clinically significant GI bleeding*
        - *Hereditary or acquired coagulation defect*
        - *Age 65 years or older*

C. *Criteria for etanercept PA* – The FDA recently approved psoriatic arthritis as a new indication for etanercept (Enbrel). The Committee voted to add this indication to etanercept's PA criteria.

D. *Anakinra (Kineret)* – This is a new IL-1 receptor antagonist product with a mechanism of action similar to the TNF receptor antagonist etanercept. However, it differs from etanercept in its FDA approved indications (see Appendix A), and therefore requires a separate PA. The Committee voted to adopt the Merck Medco criteria currently in place:

1. Coverage provided for the treatment of moderately to severely active rheumatoid arthritis in patients ≥ 18 years of age.
2. Coverage provided in situations where the use of methotrexate and at least one other DMARD have failed to treat the patient's rheumatoid arthritis.
3. Coverage provided in situations where the patient has had an inadequate response to methotrexate, unless the use of methotrexate is contraindicated for the patient.
4. Benefit coverage not provided for use of anakinra in combination with etanercept or infliximab.

The Committee discussed quantity limits for anakinra, given the exiting 6-week quantity limits in the NMOP for etanercept. They felt that, given the similarities between etanercept and anakinra, it would be most appropriate to apply the same quantity limits to both drugs. The

Committee established a 6-week quantity limit was established for anakinra in the NMOP and a 4-week supply in the retail network. The reason for the quantity limit is the same for both etanercept and anakinra: potential for significant unnecessary expense resulting from discontinuation, given the extremely high unit cost of these medications.

12. SUBCOMMITTEE REPORT: PROVISION OF INJECTABLE DRUGS IN THE NMOP OR RETAIL NETWORK PHARMACIES – Tabled until the May DoD P&T Committee meeting

13. CONTROLLED DISTRIBUTION OF PEGINTERFERON ALFA 2B (PEG-INTRON; SCHERING) – LCDR Briski reported that the distribution process has been complicated due to the unexpected demand for Peg-Intron. A formal understanding with Schering has been reached. Currently, any new patients will go onto a waiting list. The wait is expected to be one to two months. All current patients will be provided product to complete their course of therapy. LCDR Briski provided an outline of the current distribution method:

- New patients should be instructed to call the Schering 800 number to get on the waiting list. The patient will be called when it is their turn to move off the list and be instructed to take their prescription to the MTF pharmacy. All new starts, as they move off the wait list, will receive product via a drop-ship to MTF mechanism, which will be billed through Prime Vendor.
- Any current patients should complete their therapy by continuing to use their current mechanism for acquiring the drug. If the patient was enrolled into the "Assured Access" program and assigned an identifying number, they should complete their course using that mechanism. Sites that have been getting the Peg-Intron drop-shipped without registering the patient should continue to do so. As the current patients using assured access identifiers complete their therapy, the need for using the numbers will also go away.
- LCDR Briski is the point of contact for distribution issues. The PEC will provide a monthly report to Schering regarding the number of MTF patients receiving Peg-Intron so Schering can reconcile this with the amount of product shipped. If an imbalance occurs, the PEC will clarify the situation by contacting the MTFs involved directly.

14. ADJOURNMENT – The meeting adjourned at 1200 hours. The next meeting will be held at the Non-Commissioned Officers Club, Fort Sam Houston, TX starting at 0800 on Wednesday, 09 May 2002. All agenda items should be submitted to the co-chairs no later than April 8, 2002.

<signed>
DANIEL D. REMUND
COL, MS, USA
Co-chair

<signed>
TERRANCE EGLAND
CDR, MC, USN
Co-chair

List of Appendices

APPENDIX A: NEWLY APPROVED DRUGS CONSIDERED FOR THE NATIONAL MAIL ORDER PHARMACY FORMULARY AND DOD BASIC CORE FORMULARY

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP and/or retail network formulary restrictions**	**BCF Status**
Valdecoxib tablets (Bextra; Pharmacia)	19 Nov 01; COX-II inhibitor for treatment of signs and symptoms of osteoarthritis (OA) and adult rheumatoid arthritis (RA), and for the pain associated with menstrual cramping	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization:** Add to (NMOP only) COX-2 inhibitor PA as modified in the Feb 02 DoD P&T Committee minutes. **Rationale for PA:** The COX-II inhibitors celecoxib and rofecoxib require prior authorization in the NMOP. The potential for inappropriate use is substantial.	Not added to the BCF **Similar BCF Drugs:** none
Frovatriptan tablets (Frova; Elan)	09 Nov 01; 5HT agonist ("triptan") for the treatment of migraine with and without aura in adults	Added to the NMOP Formulary	**Quantity Limits** 9 tablets per 30 days; 27 tablets per 90 days; consistent with existing quantity limits for other triptans **Rationale for Quantity Limits:** Clinical appropriateness concerns: potential for overuse and increased likelihood of rebound headaches **Prior Authorization** None	Not added to the BCF **Similar BCF Drugs:** Sumatriptan
Desloratadine tablets Clarinex; Schering-Plough)	21 Dec 01; non-sedating 2nd-generation antihistamine for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and older	Added to the NMOP Formulary **Note**: Closed class contract is in place for 2nd generation NSA (fexofenadine) in the MTFs, but it does not apply to the NMOP. Three other 2nd generation products are currently available through the NMOP.	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF Drugs:** Closed class contract exists for fexofenadine (Allegra) that includes BCF status.

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP and/or retail network formulary restrictions**	**BCF Status**
Anakinra injection (Kineret; Amgen)	14 Nov 01; interleukin-1 receptor antagonist administered subcutaneously for the reduction in signs and symptoms of moderately to severely active RA in adult patients who have failed one or more disease modifying antirheumatic drugs (DMARDs)	Added to the NMOP Formulary and Covered Injectables List **Note**: Etanercept for RA is included in the NMOP Covered Injectables List, subject to quantity limits and prior authorization	**Quantity Limits:** 6-weeks **Rationale for quantity limits:** Extremely high unit cost increases negative impact of premature discontinuation. **Prior Authorization** Yes, approved use of PA criteria already established by Merck Medco.	Not added to the BCF **Similar BCF Drugs:** none
Comments about anakinra injection: Can be used alone or in combination with DMARDs other than Tumor Necrosis Factor (TNF) blocking agents [etanercept (Enbrel); infliximab (Remicade)]. Potential for serious infections and neutropenia is increased when used in combination with TNF blocking agents; combination use is not authorized in current PA criteria. Injection site problems are very common (71% of patients) upon initiation of therapy.				
Triptorelin pamoate depot injection (Trelstar LA; Debiopharm/ Pharmacia)	Jun 01; injectable leutinizing hormone releasing hormone (LHRH) agonist administered every 3 months for the treatment of advanced stage prostate cancer. Product is extension of previously approved one-month product, Trelstar Depot	Added to the NMOP Formulary and Covered Injectables List **Note**: Other depot LHRH agonists (Lupron and Zoladex) are included on the NMOP Covered Injectables List. Both 1-month and 3-month products added	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF Drugs:** none
Fondaparinux injection (Arixtra; Sanofi/Organon)	11 Dec 01; injectable factor Xa inhibitor (different than a low - molecular-weight heparin [LMWH]) for the prevention of venous thromboembolism following orthopedic surgery (knee replacement, hip replacement, hip fracture repair)	Added to the NMOP Formulary and Covered Injectables List **Note**: Injectable LMWHs are included on the NMOP Covered Injectables List	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF Drugs:** none
Comments about fondaparinux injection: The Committee discussed the fact that the current BCF mandates MTFs to have at one LMWH (enoxaparin, dalteparin, tinzaparin) on their formulary; individual MTFs choose which LMWH to have on formulary. Fondaparinux is not a LMWH and is not yet approved for outpatient treatment of VTE. The Committee determined that fondaparinux would not be considered a suitable substitution for one of the other LMWH products.				

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP and/or retail network formulary restrictions**	**BCF Status**
Pimecrolimus 1% cream (Elidel; Novartis)	13 Dec 01; treatment of mild to moderate atopic dermatitis in patients aged two years and older	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF Drugs:** See comments
Comments about Pimecrolimus 1% cream: There are no non-steroidal topical immunomodulators (TIMS) currently on the BCF. The BCF does include a medium potency steroid agent (triamcinolone acetonide 0.1% cream; Kenalog) and a high potency steroid agent (fluocinonide 0.05% cream; Lidex).				
Diclofenac sodium topical gel (Solaraze; Sky Pharma)	23 Oct 00; treatment of actinic keratoses; topical NSAID	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF Drugs:** None
Dexmethyl-phenidate tablets (Focalin; Novartis)	13 Nov 01; d-isomer of methylphenidate administered twice daily for the treatment of attention deficit hyperactivity disorder; not an extended or sustained release product	Added to the NMOP Formulary	**Quantity Limits** Standard NMOP rule for Schedule II products for treatment of ADHD applies– up to 90 day supply, no refills **Rationale for Quantity Limits: F**alls under standard rule in NMOP for Schedule II products for treatment of ADHD **Prior Authorization:** None	Not added to the BCF **Similar BCF Drugs:** Methylphenidate, methylphenidate SR and methylphenidate extended release (Concerta)
Comments about dexmethylphenidate tablets: The pharmacokinetic properties of the isomer are sufficiently different such that the FDA considers dexmethylphenidate to be a new drug. Therefore, it should not be considered the same as methylphenidate. There is no evidence that this is a significant advance in therapy for ADHD. A head-to-head trial against other forms of methylphenidate (instead of placebo) would help to clarify its place in therapy. It is specifically excluded from the BCF listing for methylphenidate.				

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP and/or retail network formulary restrictions**	**BCF Status**
Bosentan tablets (Tracleer; Actelion)	20 Nov 01; non-selective endothelin receptor antagonist for the treatment of pulmonary artery hypertension	NOT Added to the NMOP Formulary **Note**: Not feasible to provide bosentan through the NMOP due to its restricted distribution process	**Quantity Limits** N/A **Prior Authorization** Need to coordinate with TRICARE	Not added to the BCF **Similar BCF Drugs:** none
Comments about bosentan tablets: Although bosentan will be used in only a limited number of patients; it needs to be available to DoD beneficiaries. There are approximately 1,900 patients in the DoD with a diagnosis of PAH, but the severity of disease cannot be determined. Bosentan cannot be added to the NMOP due to the closed distribution system initiated by the manufacturer. The limited distribution system is due to the potential toxicities (hepatic and fetal) of this agent. Bosentan will be made available upon referral from specialty care physicians. When the distribution process is finalized, it will be disseminated via the service pharmacy consultants.				
Lovastatin/niacin tablets (Advicor; KOS)	18 Dec 01; combination of a statin and extended release niacin for the treatment of 1° hypercholesterolemia and mixed dyslipidemia who require additional lipid modification for LDL and HDL cholesterol and triglycerides beyond that achieved by the individual components	NOT Added to the NMOP Formulary	**Quantity Limits** N/A **Prior Authorization** N/A	Not added to the BCF **Similar BCF Drugs:** Closed class contract exists for simvastatin (Zocor)
Comments about lovastatin/niacin tablets: Addition of Advicor to either the BCF or NMOP formulary would be a violation of the simvastatin contract. Advicor should be available through the NMOP only in cases of documented medical necessity.				
Extended phenytoin sodium, 200 mg and 300 mg capsules (Phenytek; Bertek)	6 Dec 01; New branded generic formulation of phenytoin sodium indicated for the treatment of generalized tonic-clonic and complex partial seizures and prevention and treatment of seizures during or following neurosurgery 200 and 300 mg Phenytek capsules are bioequivalent to 2 and 3 Dilantin 100-mg capsules, respectively	Automatic addition to NMOP Formulary as line extension	**Quantity Limits** General rule applies **Prior Authorization** None	Need to clarify whether the current BCF listing for phenytoin oral will include Phenytek. This issue was tabled until pricing and provider input is available.
Brimonidine tartrate ophthalmic solution (Alphagan P; Allergan**)**	Reformulation of brimonidine tartrate ophthalmic solution with a different preservative, a lower concentration of brimonidine, and a modified pH	Added to the NMOP Formulary Conversion from Alphagan 0.2% to Alphagan P 0.15% is expected due to the planned phase out of Alphagan P 0.2%.	**Quantity Limits** General rule applies **Prior Authorization** None	Added to the BCF **Clarification:** The BCF listing will be clarified to identify brimonidine 0.15% (Alphagan P) as the specific agent on the BCF for the reasons outlined in the comments below.
Comments about brimonidine tartrate ophthalmic solution: Alphagan P 0.15% provides comparable IOP-lowering efficacy to Alphagan 0.2% (potentially due to increased bioavailability of the purite formulation as demonstrated in animal studies). No clinically significant differences were found in mean IOP or mean change from baseline in IOP between the two formulations. The incidence rate of allergic conjunctivitis in the Alphagan P 0.15% group was 41% less than in the Alphagan 0.2% group. Both products are used BID 95% of the time vs. the TID package insert recommended dosing. Company plans on phasing out the Alphagan 0.2%.				

APPENDIX B: COMBINED SUMMARY OF FORMULARY CHANGES FROM THE DOD P&T EXECUTIVE COUNCIL MEETING AND THE DOD P&T COMMITTEE MEETING

1. **BCF CHANGES**

   A. *Additions to the BCF*

      1) Advair (fluticasone/salmeterol) Inhaler: all strengths

      2) Prempro (conjugated estrogen and medroxyprogesterone): all strengths.

      3) Zithromax (azithromycin) 250 mg tablets, does not require the Z-pak dosage formulation.

      4) Plavix (clopidogrel) *[NOTE: Clopidogrel added to Appendix B subsequent to the initial release of these minutes on 8 Mar 2002. Please see Section 11 of the Feb 02 DoD P&T Executive Council meeting minutes.]*

   B. *Deletions from the BCF*

      None

   C. *Changes and clarifications to the BCF*

      1) The current BCF listing for brimonidine tartrate ophthalmic solution was clarified to identify the new Alphagan P 0.15% formulation as the specific agent included on the BCF.

2. **NMOP FORMULARY CHANGES**

   A. *Additions to the NMOP Formulary* (See Appendix A for details)

      1) Valdecoxib tablets (Bextra; Pharmacia) – added to NMOP with PA criteria

      2) Frovatriptan tablets (Frova; Elan) – quantity limits apply, see below

      3) Desloratadine tablets (Clarinex; Schering-Plough)

      4) Anakinra injection (Kineret; Amgen) –added to NMOP Covered Injectables List with PA criteria, quantity limits apply, see below

      5) Triptorelin pamoate depot injection (Trelstar LA; Debiopharm/Pharmacia) – added to NMOP Covered Injectables List

      6) Fondaparinux injection (Arixtra; Sanofi/Organon) – added to NMOP Covered Injectables List

      7) Pimecrolimus 1% cream (Elidel; Novartis)

      8) Diclofenac sodium topical gel (Solaraze; Sky Pharma)

      9) Dexmethylphenidate tablets (Focalin; Novartis) – quantity limits apply, see below

      10) Extended phenytoin sodium, 200 mg and 300 mg capsules (Phenytek; Bertek) – automatic line extension

      11) Brimonidine tartrate ophthalmic solution (Alphagan P; Allergan) - with natural attrition from Alphagan 0.2% to Alphagan P 0.15%

   B. *Exclusions from the NMOP Formulary*

      1) *Bosentan (Tracleer; Actelion)* - excluded from the NMOP due to closed distribution system initiated by the manufacturer.

2) *Lovastatin/niacin (Advicor; KOS) sustained release tablets* – lovastatin is currently excluded as a formulary agent due to existing statin contract (simvastatin) that is in effect through Feb 02.

C. Clarifications to the NMOP Formulary

None

3. **QUANTITY LIMIT CHANGES (NMOP AND RETAIL NETWORK)**

A. Quantity limit for frovatriptan tablets: 9 tablets per 30 days; 27 tablets per 90 days; consistent with existing quantity limits for other triptans.

B. Quantity limit for anakinra injection (Kineret; Amgen): NMOP: 6 packs of 7 syringes per 6 weeks; Retail: 4 packs of 7 syringes per 4 weeks.

C. Quantity limit for dexmethylphenidate tablets: Standard NMOP rule for Schedule II controlled products for treatment of ADHD applies – up to 90 days supply, no refills

4. **CHANGES TO THE PRIOR AUTHORIZATION PROGRAM (NMOP AND RETAIL NETWORK)**

A. *Etanercept (Enbrel)* -The FDA recently approved psoriatic arthritis as a new indication for etanercept (Enbrel). The Committee voted to add this indication to etanercept's PA criteria.

B. *COX-2 Inhibitors* - The Committee voted to have the same PA criteria apply to all COX-2 Inhibitors. See Section 11B for revised PA criteria.

C. *Anakinara (Kineret)* - The Committee voted to adopt the Merck Medco criteria currently in place. See Section 11D, of minutes for PA criteria.

Department of Defense
Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **12 February 2002**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Executive Council Meeting

1. The DoD P&T Executive Council met from 0800 to 1600 hours on 12 February 2002 at the Non-Commissioned Officers Club, Fort Sam Houston, TX.

2. MEMBERS PRESENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL John R. Downs, MC	Air Force
COL Mark Nadeau, MC (Representing COL Bill Sykora, MC)	Air Force
LtCol (select) George Jones, BSC	Air Force
CAPT (select) Matt Nutaitis, MC	Navy
CDR Kevin Cook, MSC	Navy
MAJ Brett Kelly, MS	Army
LTC (P) Joel Schmidt, MC	Army
CAPT Robert Rist	Coast Guard
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
Dick Rooney	Department of Veterans Affairs

MEMBERS ABSENT

COL Rosa Stith, MC	Army
LTC Mike Kieffer, MS	Joint Readiness Clinical Advisory Board

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
CAPT Betsy Nolan, MSC	Navy Pharmacy Specialty Leader
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
LtCol Ed Zastawny, BSC	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC	DoD Pharmacoeconomic Center
LCDR Ted Briski, MSC	DoD Pharmacoeconomic Center
LTC Don De Groff, MS	DoD Pharmacoeconomic Center
LTC (P) Doreen Lounsbery, MC	DoD Pharmacoeconomic Center
LtCol (select) Barb Roach, MC	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
Dave Bretzke	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
SFC Agustin Serrano	DoD Pharmacoeconomic Center
CAPT Andy Meadows, USAF	Lead Agent Region 6
Leticia Ramirez	Pharmacy Student, University of Texas at Austin Pharm.D. Program
MAJ Cheryl Filby, MS	Defense Supply Center Philadelphia
Paul Vasquez	Defense Supply Center Philadelphia
CDR Brian Kerr, MSC	Defense Supply Center Philadelphia
Vincent Valinotti	Defense Supply Center Philadelphia

3. REVIEW MINUTES OF LAST MEETING / ADMINISTRATIVE ISSUES

The Council approved the minutes of the last meeting with a correction in the last sentence of the fourth paragraph in section 10:

- Incorrect sentence: The percentage of *fatal bleeding episodes* was 2.2% for clopidogrel plus aspirin compared to 1.8% with aspirin plus placebo (a statistically non-significant difference).
- Corrected sentence: The percentage of *life-threatening bleeding episodes* was 2.2% for clopidogrel plus aspirin compared to 1.8% with aspirin plus placebo (a statistically non-significant difference).

4. ADVANCES IN MEDICAL PRACTICE (AMP) PROGRAM

AMP funds will not be used to reimburse MTF pharmacies for pharmaceutical purchases in FY 02 because Program Budget Decision (PBD) 812 is supposed to provide sufficient funding for MTF pharmacies. PBD 812 provides MTF pharmacies with 15% more funding in FY 02 than was actually spent in FY 01.

5. NATIONAL PHARMACEUTICAL CONTRACTS AND BLANKET PURCHASE AGREEMENTS (BPAs)

A. *Contract awards, renewals, and terminations*

- Contracts for Diltiazem XR, acetaminophen tablets, levobunolol ophthalmic solution, timolol ophthalmic solution, clotrimazole cream, and simvastatin were renewed.
- Contract for gemfibrozil was cancelled due to the manufacturer not being able to meet the terms of the contract.
- New contracts were awarded for cyclobenzaprine tablets, isosorbide dinitrate tablets, loperamide capsules, methocarbamol tablets, metoprolol tablets, verapamil immediate release tablets, and lactulose syrup, nitroglycerin patch, and glyburide micronized tablets.
- DoD contracts for lisinopril and hepatitis A are up for renewal.
- Joint DoD/VA contracts up for renewal: salsalate tablets, oral contraceptives, etodolac, fexofenadine, hydrochlorothiazide, insulin needle/syringes, isosorbide mononitrate, prednisone, capsaicin cream, cimetidine, ticlopidine, nicotine patches, and valproic acid.

B. *Status of Contracting Initiative for Leutinizing Hormone Releasing Hormone (LHRH) agonists* – CAPT Torkildson reported that the joint VA/DoD solicitation to select an LHRH agonist (for the treatment of prostate cancer only) has still not been released, pending completion of the update to the VA clinical review. The VA and AstraZeneca have agreed to further extend the VA's contract for Zoladex until such time as the joint VA/DoD contract has been awarded. AstraZeneca and TAP have indicated that the DoD Blanket Purchase Agreements (BPAs) for Zoladex and Lupron will remain in place until the new contract is awarded.

CAPT Torkildson presented an assessment of the clinical significance of the entry of triptorelin (Trelstar) into the LHRH agonist marketplace. Debio Recherche Pharmaceutique manufactures this agent in Switzerland; Pharmacia holds the marketing rights in the United States. This is another LHRH agonist that has been in use in Europe since 1985. The FDA approved the 1-month depot in June 2000; the 3-month depot was approved in June 2001. Both preparations are approved for the treatment of advanced prostate cancer. Unlike leuprolide and goserelin, triptorelin has no additional FDA-approved indications, although it is used in other countries for many of the same indications. Pharmacia has not yet begun marketing this product extensively in the United States. However, a company representative has indicated that they intend to bid on the joint VA/DoD LHRH agonist contract.

Two major clinical concerns have been raised regarding triptorelin. The first relates to the paucity of clinical trial data available for this agent. The majority of published reports were conducted and published in Europe in the mid to late 1980s. The primary study submitted for approval of the 3-month depot was an unpublished study that took place in South Africa. There are also no survival studies; efficacy was measured using the surrogate endpoint of a reduction in serum testosterone levels established as being equivalent to those seen following surgical castration. The second concern relates to the

drug's ability to continue to suppress testosterone production with repeated dosing, the so-called "acute on chronic effect". Following the initial dose of LHRH agonists, there is a surge in testosterone production that produces a disease flare in a small percentage of patients. This surge is followed by a predicable fall in serum testosterone concentrations to castrate levels. However, with some agents a second surge in testosterone production is seen following the second dose of the agent. This has led the FDA to require manufacturers of LHRH agonists to submit data with their approval applications regarding the likelihood that their product will induce this effect. Data were submitted for only 15/151 subjects enrolled in the South African trial noted above, 2/15 had secondary surges in testosterone levels above the acceptable level. As a result, in its approval letter the FDA has required the company to conduct a Phase IV pharmacology study to determine if this ratio is observed with a larger group of patients. While the clinical significance of this observation is unknown, it does create a concern regarding the ability of this agent to maintain serum testosterone levels within the range defined as acceptable.

The Council shared the concerns raised during the presentation, and voted unanimously that triptorelin should not be considered therapeutically equivalent to leuprolide and goserelin at this time. Triptorelin should not be included in a solicitation for a contract for an LHRH agonist for the treatment of prostate cancer.

C. *Non-sedating antihistamine contract* – Lt Col Zastawny informed the Council that prescriptions for fexofenadine (Allegra) continue to outnumber prescriptions for loratidine (Claritin) by a 9 to 1 margin at MTF pharmacies. The weighted average cost per tablet/capsule for non-sedating antihistamines purchased by MTFs in Dec 01 was $.53, which is 39% below the $.87 weighted average cost that existed prior to the contract.

According to Aventis, the 500 count bottles of both the 60 and 180 mg tablets will be added and the 60 mg capsules will be removed from the non-sedating antihistamine contract effective 28 Feb 2002. The contract price for the 60 mg and 180 mg tablets remains unchanged at $0.37 and $0.60 per tablet, respectively.

Cetirizine (Zyrtec) costs MTF pharmacies $.95 per day compared to only $.60 per day for fexofenadine 180 mg. MTFs fill almost as many prescriptions for cetirizine as for fexofenadine. The Council agreed that the PEC should publish an article in the PEC Update to encourage greater utilization of fexofenadine.

The FDA recently approved desloratadine (Clarinex). Desloratadine cannot be added to the BCF or MTF formularies while the contract for fexofenadine is in effect.

D. *Statin Contract* – MAJ Cheryl Filby stated that the contract for simvastatin (Zocor) was renewed for the final option year (until 19 Feb 03) as the Council recommended at the November meeting. Simvastatin and atorvastatin (Lipitor) account for 95% and 3.5% respectively of the total statin prescriptions filled at MTF pharmacies, but atorvastatin accounts for a much higher percentage at a few MTFs. An analysis of prescription data also revealed that the majority of atorvastatin prescriptions are filled for the 10 mg and 20 mg strengths. Higher dosages of atorvastatin (40 mg and 80 mg) would normally be needed if atorvastatin were used primarily for patients who failed to reach their LDL

goals on simvastatin. The PEC will provide statin usage data to MTFs and publish an article in the PEC Update that addresses the appropriate use of non-contracted statins.

E. *Status of contracting initiative for nasal corticosteroid inhalers* - The Council reiterated that neither flunisolide nor budesonide would be acceptable as the only nasal corticosteroid on the BCF because they too frequently require dosing more than once daily. The Council agreed that DoD could participate in a solicitation that may result in the addition of flunisolide or budesonide to the BCF, but neither of these drugs can be the sole nasal corticosteroid on the BCF.

F. *Potential contracting initiative for carbamazepine* – There is an opportunity to establish a joint VA/DoD single-source contract for an AB-rated generic carbamazepine. A recent analysis of carbamazepine purchases by DoD MTFs revealed that 85% of purchases were for branded Tegretol, at 5 times the cost of the available generics.

At the last DoD P&T Executive Council meeting, the PEC was asked to query the field and evaluate why there is high usage of brand name Tegretol when AB-rated generics are available. The Council also wanted a sense of how providers and pharmacists in the field would view a generic contract for this drug.

Responses were received from 35 primary care providers, pharmacists and neurologists. The majority of respondents (77%) were not concerned about whether the drug provided at their facility was generic or brand name. They agreed that Tegretol was prescribed because they were confident it would always be supplied by the same manufacturer. This guaranteed that the color, shape, etc. of the tablet would remain constant so as not to confuse patients or bring up questions of differences in bioavailability. Many also noted that carbamazepine is typically not the drug of choice for treating seizure disorders since safer options are now available. The drug is being used frequently for neuropathic pain control, where bioequivalence does not carry the same significance as it might for seizure control. However, since there is still some use as an antiepileptic, respondents felt a contract for an AB-rated generic would be acceptable, as long as a single manufacturer was chosen for a long-term contract to maintain consistency.

The Council learned that the proposed contract would allow facilities to use either the contracted generic or brand name Tegretol. The Council recognized that this conflicts with the desire of DoD providers to stipulate the use of a single carbamazepine product throughout the MHS. Some Council members asserted that this situation was still preferable to the current situation in the DoD, where all five generic products are currently being utilized. They also recognized the value in participating with the VA in a contracting action for this agent, and felt that it would be a first step in working toward the goal of all facilities using the contracted agent exclusively. After much discussion, the Council voted to support a joint VA/DoD solicitation for a single source of generic carbamazepine that allows MTFs to use either the contracted generic carbamazepine or brand name Tegretol (assuming that Tegretol does not in fact win the contract).

a. *Compliance with sole source contracts* - LCDR Ted Briski reported that a review of generic contract compliance revealed many instances where MTFs purchased non-contracted products. A small sampling of MTF pharmacy directors indicated that unavailability of the contracted product from the prime-vendor caused MTFs to purchase

non-contracted products. The Council views unavailability of contracted products as a patient compliance/safety issue since it may cause patients to receive different looking tablets or capsules each time they receive a prescription. LCDR Briski and Dave Bretzke will coordinate with MAJ Cheryl Filby to assess the problem and report back at the next meeting.

G. *Potential contracting initiative for fluoroquinolones* – Levofloxacin is currently on the BCF in accordance with a BPA. The Council concluded in Nov 01 that levofloxacin and gatifloxacin are therapeutically interchangeable and that either agent would be clinically acceptable as the "workhorse" oral fluoroquinolone. Ortho-McNeil has offered a modified BPA to both DoD and the VA, which removes the market share requirements and gives a uniform price of $2.00/tab system-wide. The BPA would reduce overall expenditures while avoiding the logistical and economic consequences of undergoing a product conversion that could potentially result from a contracting action. However, the Council also believes that it is still clinically acceptable to participate in a joint DoD/VA contract. Since the clinical needs of patients could be satisfied with either a contract or a BPA, the Council voted to support whichever joint action the VA/DoD contracting workgroup decides to pursue.

H. *Potential contracting initiative for triptans* – Lt Col Zastawny presented information from clinical studies and provider input regarding triptans. Clinical studies show that triptans generally will provide pain relief within 2 hours for 50-75% of patients and that 25-40% of patients will be pain free after two hours. One study showed that 45-58% of patients who did not respond to the initial triptan would respond to a different triptan. The clinical trial data suggest that patients' clinical needs would not be satisfied if a contract prohibited MTFs from having more than one triptan on their formularies. The majority of MTF providers surveyed by the PEC agreed that a contracting action would not be acceptable if it limited MTF formularies to a single triptan. The Council voted to support any contracting initiative or other pricing agreement that either allows or requires MTFs to have at least two triptans on their formularies.

I. *Potential contracting initiative for angiotensin receptor blockers (ARBs)* – LCDR Briski reported that MTF expenditures for ARBs increased from $5.7 million in FY 99 to $14.5 million in FY 01. The VA and DoD are working together on a clinical review of the ARBs. The PEC will forward the clinical review to Council members and compile additional information that will assist the Council in assessing the need for addition of an ARB to the BCF and the therapeutic interchangeability of the ARBs for a potential contracting initiative.

J. *Other contracting initiatives:* According to prime vendor data, national pharmaceutical contracts produced $16 million in cost avoidance at MTFs during the first quarter of FY 02. As for the third and fourth quarters of FY 01, prime vendor data for the first quarter of FY 02 are missing for many MTFs, so the actual cost avoidance is more than $16 million. Through Dec 01, the weighted average cost per unit for drugs covered by national pharmaceutical contracts is 33% less than the weighted average cost per unit that existed before the contracts took effect. Although MTFs are now spending much less for

proton pump inhibitors, no cost avoidance is attributed to this drug class because there is no contract in effect for proton pump inhibitors.

6. POTENTIAL IMPACT OF NEW GENERICS

A. *Fluoxetine:* CAPT Torkildson presented an update on the situation regarding generic fluoxetine. Barr Pharmaceuticals' 6-month period of exclusivity for this product expired in late January. On January 29 the FDA approved several additional generic fluoxetine products. At least two companies receiving approval have submitted the necessary paperwork to establish FSS pricing for their generic products. The prices contained in the most recent FSS pricing database for these products range from $4.49 to $5.19/100 capsules for the 10 mg and 20 mg strengths. It is uncertain at this time how soon these prices will be loaded or when they will be available to the MTFs, but they will likely be available by March 1. MTFs are advised to examine the available prices carefully before purchasing quantities of fluoxetine in the near future. If MTFs transition quickly to these significantly less expensive generic products, it is anticipated that the MHS could reduce expenditures for fluoxetine by as much as $13M over the next 12 months.

B. *Metformin:* The FDA approved generic formulations of metformin (Glucophage) on 25 Jan 01. At least six generic companies will market metformin, and five of them have approval for all three strengths (500-, 850-, and 1000 mg). The extended release metformin preparation (Glucophage XR) and combination product with glyburide (Glucovance) are still under patent.

Current FSS prices for Glucophage are $0.32 for the 500 mg tablet, $0.55 for the 850 mg tablet, and $0.58 for the 1000 mg tablet. MTFs spent approximately $20 million on Glucophage during the past 12 months. While FSS prices have not yet been established for generic metformin, a hypothetical example can illustrate the magnitude of potential cost savings. For example, MTFs could potentially save about $15 million annually if the generic metformin price is 75% less than the Glucophage price.

7. SUBCOMMITTEE REPORT: OBTAINING INPUT FROM PROVIDERS

LCDR Briski reported on the latest efforts by the PEC staff to obtain input from MTF-based providers, which is an important factor in pharmaceutical contracts and formulary management. The email groups put together by MAJ Roach have been effective, but do not reach all MTFs. Since the DoD P&T is a TMA chartered organization, using the TMA infrastructure is a logical mechanism to communicate with MTFs. The PEC initiated monthly teleconferences with lead agent medical directors and lead agent pharmacists. The PEC's goal is to tap into the already existing networks these senior Lead Agency staffers have established. Close contact with the service-specific chains of command will continue to be maintained via the Chief Pharmacy and Chief Clinical Consultants to each Surgeon General. In addition, the PEC is exploring the options for creating a Chat room/Bulletin Board section of the PEC web site to facilitate consistent and timely communication. P&T minutes will continue to be distributed through service and TMA lanes.

8. MTF REQUESTS FOR BCF CHANGES

A. *Request to add Advair (fluticasone/salmeterol) to the BCF* – An Air Force allergist provided the following rationale for the request:

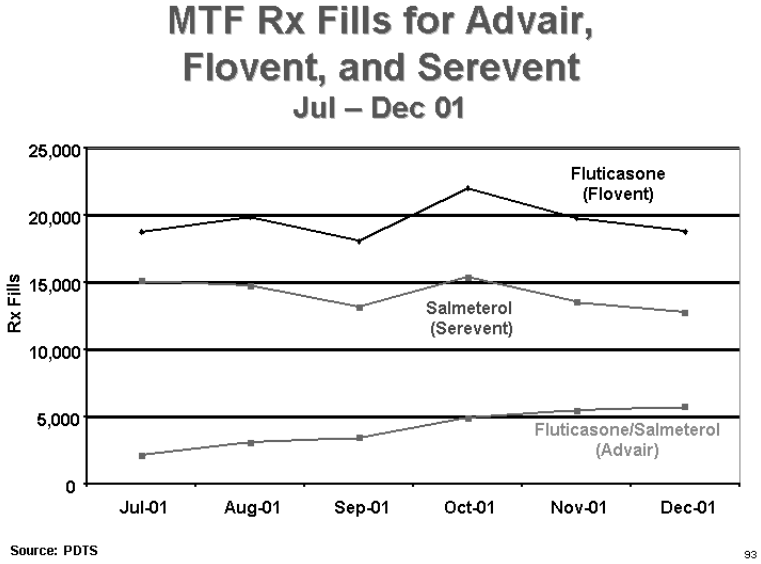
- Nine studies have proven that the addition of a long acting beta-agonist is superior to doubling the dose of inhaled corticosteroid (ICS) in the treatment of uncontrolled asthma in the patient already on an ICS.
- The evidence also suggests that long acting beta-agonists should never be used as mono-therapy and should always be used in conjunction with ICS.
- Compliance with asthma controller medication decreases when more than one inhaler is used.
- Advair offers mandatory combination therapy and a single inhaler of 1 puff twice a day (vs. 2 inhalers, 4 puffs twice a day).

Safety and tolerability of the combination product are similar to the same dosages of the products administered by separate inhalers. The FDA allowed the removal of the box warning about adrenal insufficiency surrounding the use of inhaled corticosteroids class because no cases were reported. Efficacy of the combination product is similar to the same dosages of the products administered by separate inhalers. An article by Aubier et al. comparing Advair vs. the two single agents demonstrated that the two arms were equal for morning Peak Expiratory Flow (PEF).

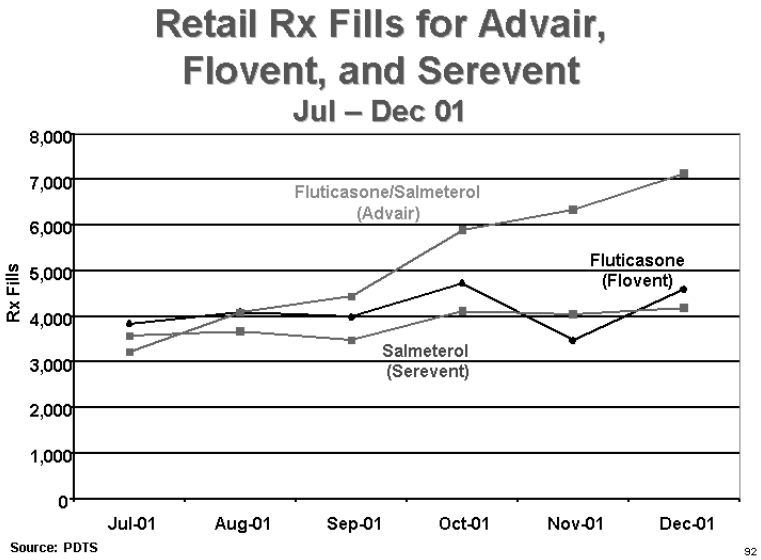
The PEC requested provider (physician and pharmacist) input on this issue and received 63 responses: 56 favoring addition to the BCF; 4 against addition to the BCF; and 3 inconclusive regarding addition of Advair to the BCF. Providers made several key points:

- Advair provides perceived symptom improvement within 30 minutes (from the Serevent). Researchers have speculated that the patient's perception of the benefit of the treatment rather than the dosage form itself may be the more critical factor. Some patients using the separate inhalers will identify Serevent as the agent that causes improvement, stop the inhaled steroid, and then end up on Serevent monotherapy. One large MTF survey showed that 200 patients were on Serevent monotherapy.
- The greatest benefit would be to our teenage population. The death rate of asthma in children has risen 150% between 1980 and 1996 – the age group with the highest mortality is 15-24 years of age. Asthma deaths today are preventable and we need to support combination therapy of inhaled corticosteroids and long-acting beta-agonists.
- Advair can be administered in 1/20 of the time it takes to use the 2 separate inhalers. How could this not improve compliance?

Fluticasone and salmeterol are on the BCF as individual agents. As shown in the following graph, prescription fills for Advair are rising steadily at MTFs (up 60% from Jul 01 to Dec 01), while usage of the individual agents is flat or declining slightly.



Prescription fills for Advair are rising even faster in the retail network pharmacies (more than doubled from Jul 01 to Dec 01)



The FSS pricing as of January 2002 for Advair and the individual products is presented in the following table:

Item Description		Doses/container	FSS Price As of Jan 2002
Advair Diskus Inhaler	fluticasone 100 mcg/salmeterol 50 mcg	60	$64.27
	fluticasone 250 mcg/salmeterol 50 mcg	60	$80.54
	fluticasone 500 mcg/salmeterol 50 mcg	60	$102.82
Serevent	salmeterol 25 mcg MDI	120	$42.72
	salmeterol 50 mcg diskus	60	$45.32
Flovent	fluticasone 110 mcg MDI	120	$39.60
	fluticasone 220 mcg MDI	120	$60.10

The cost of Advair is compared to the cost of the individual products in the following table:

Item Description	Advair cost/day Using twice daily dosing	Cost/day for equivalent dose of individual products	Additional cost per day for Advair
fluticasone 100 mcg/salmeterol 50 mcg	$2.14/day	$2.09/day	$0.05/day
fluticasone 250 mcg/salmeterol 50 mcg	$2.68/day	$2.43/day	$0.25/day
fluticasone 500 mcg/salmeterol 50 mcg	$3.43/day	$3.43/day	$0.00/day

Addition of Advair to the BCF could improve patient satisfaction and compliance. There is also a potential reduction in waste, since most fluticasone and salmeterol use is of MDI inhalers that are hard to estimate remaining doses. Advair Diskus gives number of doses remaining. The Council added all strengths of the fluticasone/salmeterol (Advair) to the BCF.

B. *Request to add Plan B (emergency contraceptive) to the BCF* – An MTF provider offered the following rationale in support of the request:

- Use of an emergency contraceptive is the only method available to prevent pregnancy after unprotected sexual intercourse or after a contraceptive "accident."

- It can provide emergency treatment for victims of sexual assault who were not protected by an effective contraceptive.
- A couple or a single female may suffer economic hardship as well as significant psychological and social costs from an unintended pregnancy.
- Although relatively higher in cost than some combination formulary contraceptives, the cost of Plan B is well within the range of the most commonly used preparations for this purpose, and the volume or frequency of use would be relatively low.
- The lower side effect profile of Plan B would decrease the use and cost of anti-emetics usually prescribed with the combination regimens, and the cost and necessity of return visits for adverse effects or therapeutic failure.
- The greater clinical efficacy, lower adverse effects, and simplified patient dosing regimen make Plan B the drug of choice for emergency contraception.
- Data indicate a rapid return of normal ovulation and fertility following discontinuation of either combined estrogen-progestin or progestin-only tablets for emergency contraception.
- Emergency contraceptives should be uniformly and immediately available in order to maximize their effectiveness in preventing unintended pregnancies and thereby reducing the number of women who seek elective abortions.

The Council considered the following information regarding emergency contraceptives in general and Plan B in particular:

- The American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Family Practice (AAFP) recommend and endorse the use of emergency contraception.
- ACOG estimates that use of emergency contraceptives could prevent as many as half of the approximately 3 million unintended pregnancies that occur each year in the United States, including as many as 700,000 pregnancies that are terminated by abortion.
- Emergency contraception counseling should be provided during every annual health maintenance examination per BUMED NOTE 6320 (26 Oct 99) and Article 15-76 of the Manual of the Medical Department, Section VI; Family Planning, Contraceptive Counseling, and Sexually Transmitted Disease Prevention Counseling.
- The OB/GYN consultants for the three services support the addition of Plan B to the BCF.
- Ethics consultants for the three services concluded that there are no apparent reasons to preclude the use of Plan B at MTFs, since it is an FDA-approved contraceptive and not, as some argue, an abortifacient. Service regulations and TRICARE policy do not prohibit the coverage of emergency contraceptives. The presence of Plan B on the BCF would not "force" providers to prescribe Plan B. As with all other drugs on the BCF, the decision to prescribe Plan B would be left to the discretion of the individual provider.
- MTFs already provide emergency contraceptive therapy. Most MTFs use regular oral contraceptives in an "off label" fashion, while some MTFs use Plan B.
- The first dose of an emergency contraceptive should be taken within 72 hours of unprotected sex, preferably during the first 24 hours, followed by a second dose 12 hours later. The earlier the emergency contraceptive is given, the more likely it is to prevent pregnancy. The need for timely administration supports the argument that the emergency contraceptive should be on the MTF formulary in order to preclude delays that might

occur if the medication had to be obtained through a non-formulary or special order request.

- MTF providers and pharmacists responded to a survey regarding the proposal to add Plan B to the BCF. 38 respondents supported the addition, 15 respondents did not support the addition, and 14 respondents did not clearly express their position.
- Plan B is more efficacious than the Yupze regimen (ethinyl estradiol 100 mcg and levonorgestrel 0.5 mg taken twice, twelve hours apart). A large-scale clinical trial conducted at 21 treatment centers in 14 countries found a pregnancy rate of 1.1% (95% CI 0.6-2.0) for Plan B versus a pregnancy rate of 3.2% (95% CI 2.24.5) for the Yupze regimen.
- The incidence of nausea and vomiting associated with Plan B is less than half the incidence of nausea and vomiting associated with the Yupze regimen.
- The Plan B regimen requires the patient to ingest a total of 2 tablets, which is much more tolerable than the 20 tablets that a patient must ingest when using progestin-only tablets.
- The costs per regimen of the various emergency contraceptive alternatives are:
    - Plan B: $11.63
    - Preven: $3.91
    - Yupze regimen: $9.92
    - Progestin-only tablets (norethindrone): $9.20

The Council voted to add Plan B to the BCF. However, the Council decided that the addition of Plan B to the BCF would not be official until the Council verifies with TMA that this action is consistent with existing DoD policy.

9. REVIEW OF BCF

A. *Follow-up of anxiolytic review – potential BCF addition of venlafaxine extended release (Effexor XR)* – The Council recommended tabling this topic until the meeting in May.

B. *Analysis of midday dosing with methylphenidate dosage forms.* The following table displays the results of analyses of midday dosing associated with random samples of methylphenidate-SR prescriptions filled between Oct 99 and Sep 00 and Concerta prescriptions filled between Oct 00 and Dec 01.

Midday Dose	Methylphenidate-SR Rxs	Concerta Rxs
Yes	78 (40%)	17 (8%)
No	115 (60%)	178 (92%)
Total	193 (100%)	195 (100%)

The analyses indicate that the addition of Concerta to the BCF improved a humanistic outcome of drug therapy by decreasing the frequency of midday dosing of methylphenidate products for ADHD patients.

C. *Potential additions to BCF based on usage review*: Medications reviewed for BCF addition based usage criteria/analysis: 1) Top 200 list from PDTS; 2) High use in retail network; 3) Significant formulary status at MTFs; and 4) High dollar items.

- *Conjugated estrogens/medroxyprogesterone acetate (Prempro)* – Safety, tolerability and efficacy are similar for Prempro and the same dosages of the

drugs administered as separate tablets. Most providers think that the potential for improved compliance with Prempro may increase effectiveness. Based on prime vendor data, the average daily cost of Prempro is $0.32, while the average daily cost of providing the same dosage of medroxyprogesterone and conjugated estrogens via separate tablets is $0.39, so Prempro is actually less expensive than the individual products.

Prempro 0.625/2.5 is on the formulary at 63 (59%) of 107 MTFs. Prempro 0.625/5 is on formulary at 37 (35%) of 107 MTFs. Prempro 0.625/2.5 was ranked #5 in dollars spent, #24 in prescriptions, and #53 in unique users at retail network pharmacies.

The PEC requested provider (physician and pharmacist) input. Of 141 responses, there were 108 in favor, 17 opposed, and 16 indecisive regarding the addition of Prempro to the BCF.

The Council added all strengths of Prempro to the BCF.

- *Gabapentin (Neurontin)* – Gabapentin was evaluated for potential addition to the BCF based on the fact that gabapentin was in the top 200 in PDTS, high usage rate in retail network, and is a high dollar item. MTF expenditures for FY 01 were $12 million. Anticonvulsants rank #12 in all DoD expenditures, with ½ of that being gabapentin. Gabapentin 300mg strength ranks #17 in expenditures and #69 in unique users in the retail network.

  The PEC requested provider (physician and pharmacist) input on this issue and received 55 responses: 22 favored, 11 opposed (nearly all due to cost), and 12 were inconclusive regarding the addition of gabapentin to the BCF. One provider indicated that gabapentin quickly became a staple in their pain arsenal and usage would likely increase dramatically in the next few years. Another provider commented that the most beneficial aspects of gabapentin are its lack of significant interactions, lack of hepatic metabolism, and lack of need for blood work monitoring. A Pfizer report stated that the worldwide use for pain indication is 85% and is increasing by a 55% growth rate. Since the usage of gabapentin will likely continue to increase, and it is a safe, well-tolerated alternative to other agents for neuropathic pain control, the PEC recommended addition of gabapentin to the BCF.

  Council members were concerned that gabapentin is not FDA approved for pain control and that it may pose a large cost burden to small MTFs. They were also concerned that there is very little solid literature to back its use for pain control. The company has a supplemental new drug application pending for FDA approval for treatment of neuropathic pain.

  The Council decided not to add gabapentin to the BCF.

- *Azithromycin (Zithromax)* – Azithromycin is a widely used agent proven safe and effective in a broad range of infectious processes. FSS pricing as of Jan 2002 for the 250 mg strength of azithromycin is $4.00/tablet or $25.00/5 day course. Azithromycin 250 mg tablet strength is #2 by unique users and #9 by Rx fills in

the retail network. Azithromycin is on 94% of MTF formularies. Provider input was not obtained for this product. Due to high volume in retail pharmacy network and representation on a vast majority of MTF formularies the Council added azithromycin 250 mg tablets to BCF (does not require the Z-pak dosing form).

10. AVAILABILITY AND PRICING OF ORTHO NOVUM 7/7/7

Ortho Novum 7/7/7 is listed on the BCF and has been available for purchase by MTFs through the Depot or directly from Ortho-McNeil for approximately $7.70/cycle. This price is not available to MTFs via Prime Vendor (approximately $16.00/cycle) because of the packaging of the product ("clinic" packs vs. "commercial" packs). Ortho-McNeil stated that it would not renew the Depot contract, which expires at the end of February 2002. Ortho Novum 777 will no longer be available from the Depot when existing supplies are exhausted. There has been no determination on the long-term availability of the "clinic" packs directly from the manufacturer. The PEC will continue to monitor the situation and determine whether a change to the BCF is necessary.

11. BLEEDING RISKS IN THE CURE TRIAL

The Council evaluated the results from the CURE (Clopidogrel in Unstable Angina to Prevent Recurrent Events) trial at the Nov 01 meeting in consideration of a proposal to add clopidogrel (Plavix) to the BCF. The Council noted the higher incidence of bleeding reported with the combination of clopidogrel plus aspirin vs. the placebo plus aspirin group. The definition of major bleeding used in the CURE trial differed from the widely accepted definition used by the American College of CHEST Physicians (ACCP). Council members were concerned that the number of major bleeds in the CURE trial may have been even higher if the ACCP definition had been used. The Council asked the PEC to request additional information from Bristol Myers Squibb (BMS) about the bleeding rates in the CURE trial.

The PEC sent questions to BMS on 3 Jan 2002. BMS referred the questions to the CURE trial investigators. The PEC received a response from the investigators on the evening of 11 Feb 02. The PEC did not have enough time to analyze the response prior to the 12 Feb 02 P&T Executive Council meeting. At the 12 Feb 02 meeting the Council asked the PEC to analyze the response, estimate the number of major bleeds using the ACCP definition for major bleeds, and forward the analysis and estimates to the Council members so they could vote on the proposal to add clopidogrel to the BCF and report the results of the vote as part of the minutes for this meeting.

Based on the response from the CURE investigators, the PEC estimated that the number of major bleeds in the clopidogrel plus aspirin group would increase by 6 (from 231 to 237) and the number of bleeds in the placebo plus aspirin group would increase by 9 (from 169 to 178) using the ACCP definition for major bleeds. Using the ACCP definition for major bleeds did not produce a significant change in the number of major bleeds for either group in the CURE trial. A BMS representative stated that several articles are planned for publication based on the CURE study, including one devoted to bleeding episodes. Additionally, newly updated guidelines by the American Heart Association and the American College of Cardiology are expected to recommend that clopidogrel receive a type one recommendation (the highest quality recommendation) for use in patients with non-ST segment-elevation myocardial

infarction; however, the guidelines have not yet been published. The PEC forwarded this information to the Council members, and the Council members voted to add clopidogrel to the BCF.

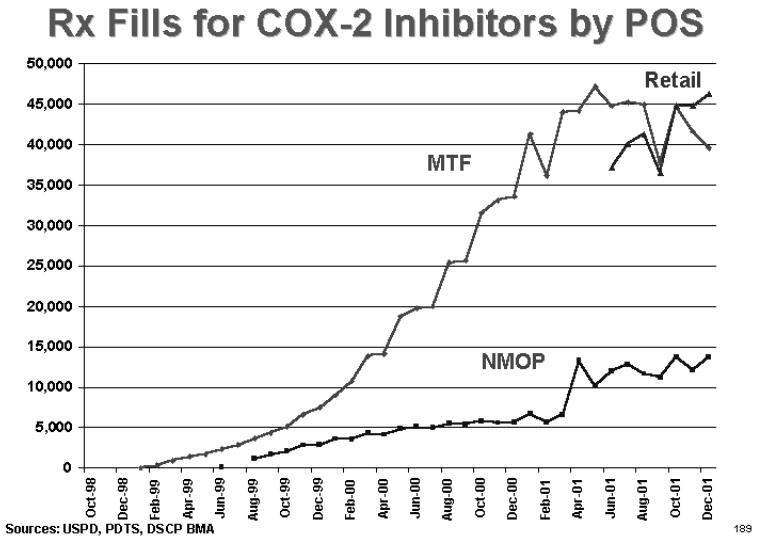
12. PROTON PUMP INHIBITORS

Rabeprazole (Aciphex) replaced omeprazole (Prilosec) on the BCF on 1 Oct 01. In Nov 01 the PEC asked MTF providers if there had been any specific problems with dosing, tolerance or patient response to Aciphex when used for common outpatient diagnoses such as GERD compared to their experience with Prilosec. Providers were also asked if the switch to Aciphex was problematic for providers, patients or pharmacists. The PEC received 41 provider responses from 32 MTFs. Most reported no problems and were very pleased with the huge decrease in the cost of proton pump inhibitor therapy. Favorable comments included the perception of a higher success rate with Aciphex and preference for the small Aciphex tablet compared to the large Prilosec capsule. A few providers reported a higher rate of treatment failures with Aciphex. One provider expressed concern about the procedure used by the MTF to convert patients from Prilosec to Aciphex.

13. COX-2 INHIBITORS

The Council considered various factors pertinent to the potential addition of a COX-2 selective inhibitor ("COX-2 inhibitor") to the BCF.

- COX-2 inhibitor usage data for the three outpatient pharmacy points of service are displayed in the graph below. After steadily increasing for 2.5 years, COX-2 prescription fills have leveled off at MTF pharmacies. COX-2 prescription fills have also leveled off somewhat in the NMOP after a sharp increase associated with the implementation of the TRICARE Senior Pharmacy Program. Limited historical data make it difficult to discern a usage trend in retail network pharmacies, but they are currently filling more COX-2 inhibitor prescriptions than MTF pharmacies.



- A survey of the COX-2 formulary status in the CHCS system at 96 MTFs revealed:
  - 41 (43%) had no COX-2 inhibitors on formulary
  - 30 (31%) had one COX-2 inhibitor on formulary
  - 25 (26%) had two COX-2 inhibitors on formulary
- Funding for MTF pharmacies in FY 02 is 15% above actual expenditures in FY 01. An objective of the increased funding is to make more drugs available at MTF pharmacies so that beneficiaries are not forced to go to a more expensive point of service (e.g. the retail network) to obtain their medications.
- Significant price reductions on certain drugs and the prospect for price reductions associated with the availability of new generic medications will substantially reduce MTF expenditures in some major drug classes, which can "free up" money for spending on other drug classes.
- A new COX-2 inhibitor, valdecoxib, is available. Approval of a fourth COX-2 inhibitor, etoricoxib, is expected in the near future. Significant price competition is unlikely at this time since the same companies that manufacture celecoxib and rofecoxib also manufacture the new agents, but more new entries in this and related drug classes are anticipated.
- The Council previously determined that celecoxib and rofecoxib are not sufficiently therapeutically interchangeable for a closed class contract.

The Council also reviewed a model constructed by the PEC that estimates the total cost to DoD of adding a COX-2 inhibitor to the BCF given assumptions about the percentage of switches from non-selective NSAIDs to COX-2 inhibitors, the absolute increase in COX-2 inhibitor prescriptions among patients not previously receiving an NSAID, the movement of COX-2 prescriptions from the retail networks to MTFs, and the anticipated percent decrease in average cost per unit for COX-2 inhibitors at MTFs and the NMOP that would result from selecting one COX-2 inhibitor for the BCF.

The Council voted that DSCP should issue a request for Blanket Purchase Agreement (BPA) price quotes to the pharmaceutical companies that market COX-2 inhibitors for the purpose of adding a COX-2 inhibitor to the BCF. The COX-2 drug class would remain "open" on the BCF. The Council will consider the price quotes, as well as the relative safety, tolerability, efficacy/effectiveness, and other relevant factors, in selecting a COX-2 inhibitor for the BCF. However, if its analysis demonstrates that it is not in the Government's best interest, the Council reserves the right to not select a COX-2 inhibitor for the BCF. The request for BPA price quotes will also ask the pharmaceutical companies to submit their plans for assisting MTFs in targeting the use of COX-2 inhibitors to the patients at greatest risk for gastrointestinal events. The Council encourages the continued use of COX-2 guidelines at MTFs in the efforts to ensure appropriate, cost-effective use of COX-2 inhibitors. The Council also requested DSCP to ask the VA if it wishes to participate in this request for BPA price quotes.

14. ADJOURNMENT

The meeting adjourned at 1600 hours on 12 Feb 2002. The next meeting will be held at the Non-Commissioned Officers Club, Fort Sam Houston, TX starting at 0800 on 8 May 2002. All agenda items should be submitted to the co-chairs no later than 8 April 2002.

<signed>	<signed>
DANIEL D. REMUND	TERRANCE EGLAND
COL, MS, USA	CDR, MC, USN
Co-chair	Co-chair