Department of Defense
Pharmacoeconomic Center

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MCCS-GPE **15 NOVEMBER 2001**

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 15 November 2001, at the Uniformed Services University of the Health Sciences, Bethesda, Maryland.

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 Bill Sykora, MC	Air Force
LtCol (select) George Jones, BSC	Air Force
CAPT (select) Matt Nutaitis, MC	Navy
CDR Kevin Cook, MSC	Navy
COL Mike Heath, MS (representing MAJ Brett Kelly)	Army
COL Rosa Stith, MC	Army
LTC (P) Joel Schmidt, MC	Army
CAPT Chuck Bruner	Coast Guard
LTC Mike Kieffer, MS	Joint Readiness Clinical Advisory Board
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
William Hudson	Humana
Ron McDonald	Sierra Military Health Services
Gene Lakey	TriWest

MEMBERS ABSENT

Dick Rooney	Department of Veterans Affairs
Ray Nan Berry	Health Net Federal Services

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
CAPT Betsy Nolan	Navy Pharmacy Specialty Leader
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
LCDR Ted Briski, MSC	DoD Pharmacoeconomic Center
LCDR Denise Graham	DoD Pharmacoeconomic Center
MAJ Cheryl Filby, MS	Defense Supply Center Philadelphia
MAJ Maria Ionescu	Pharmacy Benefits Division, TMA
Howard Altschwager	Deputy General Counsel, TMA
David Bretzke	DoD Pharmacoeconomic Center
David Chicoine	Uniformed Services Family Health Plan
Lisa Le Gette	DoD Worldwide TRICARE Information Center
Shirif Mitry	Pharmacy Student, TMA
Mark Petruzzi	Merck-Medco
David Spiler	Merck-Medco
Shana Trice	DoD Pharmacoeconomic Center
Paul Vasquez	Defense Supply Center Philadelphia

3. **REVIEW MINUTES OF LAST MEETING / ADMINISTRATIVE ISSUES** – The Committee approved the minutes of the last meeting with one correction: the entry for valganciclovir (Valcyte) on Page 8 (Appendix A) was changed to list Roche as the manufacturer rather than Syntex.

4. **INTERIM DECISIONS** – In September 2001, voting members of the Committee communicated via email and telephone to make an interim decision regarding the status of PPIs on the National Mail Order Pharmacy (NMOP) Formulary subsequent to the expiration of the omeprazole contract on 1 Oct 2001. The voting members decided to retain omeprazole on the NMOP Formulary, add rabeprazole and pantoprazole to the NMOP formulary, and exclude lansoprazole and esomeprazole from the NMOP formulary. The decision was communicated to the field in early October 2001.

5. **UNIFORM FORMULARY–** COL Davies reported that the draft rule for the Uniform Formulary was sent to the Office of Management and Budget (OMB) on 29 Oct 01. [Note: It was subsequently determined that a summary notification of the draft rule was sent to OMB on 29 Oct 01. The draft rule was not sent to OMB until 30 Nov 01.]

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 8 new drugs (see Appendix A).

7. **PROPOSED BPA FOR LANSOPRAZOLE FOR NMOP FORMULARY STATUS** - Lansoprazole (Prevacid) and esomeprazole (Nexium) are not on the NMOP formulary. TAP is offering a BPA with the following provisions if lansoprazole is added to the NMOP formulary:

   - For the first three months of the BPA (15 Nov 01 – 15 Feb 02), TAP will provide all eligible DoD MTF and NMOP facilities a $0.99 per tablet price for Prevacid.
   - Before the expiration of the first three-month period after pricing is in place, MTF and NMOP facilities must place Prevacid on their individual formularies in order to guarantee that they will continue to receive the BPA price for Prevacid.
   - If Prevacid has not been placed on individual MTF and NMOP formularies, TAP reserves the option to increase the price of Prevacid to the current published FSS price at MTFs where Prevacid is not on formulary.

   The Committee decided to place lansoprazole on the NMOP Formulary.

8. **PROPOSAL TO REMOVE OMEPRAZOLE FROM THE NMOP FORMULARY** – As of the first week in November 2001, the average cost per unit for proton pump inhibitors (PPIs) dispensed by the NMOP was $1.86, which is 72% higher than the $1.08 average cost per unit for PPIs dispensed by MTF pharmacies. MTFs and the NMOP pay the same prices for PPIs. The average cost per unit is higher in the NMOP because high-priced omeprazole continues to dominate PPI usage in the NMOP (72% of PPI prescription fills during the first week in November). Legal challenges continue to delay the availability of generic versions of omeprazole, so price relief is not imminent. A recent "Pink Sheet" article contained a prediction by a generic manufacturer that generic versions of omeprazole would not be available until the second half of calendar year 2002.

   The P&T Committee considered a proposal to remove omeprazole from the NMOP formulary. Patients who currently receive omeprazole from the NMOP would be "grandfathered" so that they could continue to receive omeprazole from the NMOP. Removal of omeprazole from the NMOP formulary would encourage the use of more cost-effective PPIs.

   Committee members and other attendees expressed concern that constraining availability of such a widely used drug could discourage patients from using the NMOP. Others were concerned that patients might simply get omeprazole prescriptions filled at retail pharmacies at a higher cost to the government and the patient. The Committee voted to retain omeprazole on the NMOP formulary.

9. **ANTIBIOTIC PROPHYLAXIS FOR ANTHRAX EXPOSURE** – The Committee discussed the recent memorandum from Health Affairs supporting Centers for Disease Control and Prevention (CDC) guidelines for antibiotics used for prophylaxis for anthrax exposure. They also reviewed data on the number of prescription fills for ciprofloxacin in the Managed Care Support Contractor (MCSC) retail networks, MTFs, and the NMOP. Although there were modest increases in the number of prescription fills for ciprofloxacin in early to mid October, utilization now appears to have returned to pre-September 11th levels. Increased usage was most notable in affected areas (Florida and Washington). The DoD P&T Committee, the PEC, and TMA will use Pharmacy Data Transaction Service (PDTS) data to monitor usage of ciprofloxacin and doxycycline (and other antibiotics that may be used for anthrax prophylaxis in the future) in MTFs, the NMOP, and the retail network.

10. PRIOR AUTHORIZATIONS

A. *Cost avoidance from NMOP prior authorizations (PAs)* – Cost avoidance analyses were not completed for this quarter due to lack of data for September 2001.

B. *Changes to PA criteria for COX-2 inhibitors* – In Oct 2001, celecoxib (Celebrex) 100 mg capsules received a supplemental indication from the Food and Drug Administration (FDA) for the management of acute pain in adults and treatment of primary dysmenorrhea. Existing NMOP PA criteria for COX-2 inhibitors allow use of rofecoxib for 20 days or less in patients with risk factors for GI adverse events, but not celecoxib, which previously lacked any indication for acute use. The Committee decided to table this issue until the next meeting when the following information is expected to be available: new package labeling for celecoxib; the percentage of rofecoxib prescriptions in the NMOP written for short-term use; and actions taken at the Jan 02 meeting of Merck-Medco's internal P&T committee (since the NMOP criteria were adapted from and are similar to criteria used by Merck Medco for other mail order clients).

C. *Clinical Rationale Statements on NMOP PA forms* – There are two versions of the NMOP PA request forms: (1) forms maintained on the PEC website for download by patients and providers, and (2) forms used internally by Merck-Medco to fax to providers when prior authorization is needed. A year ago the DoD P&T Committee decided that NMOP PA request forms should include a clinical rationale statement. The task of constructing the clinical rationale statements was delegated to the PEC staff.

   The PEC staff has encountered significant difficulties in constructing and updating the clinical rationale statements. Space is limited on the single-page forms, so it is difficult to construct complete, coherent clinical rationale statements that will fit on the forms. Any changes in the clinical rationale statements on the forms used by Merck Medco must go through a lengthy approval process.

   The Committee decided to remove the clinical rationale statements from the NMOP PA request forms, but make them available on the PEC website. The NMOP PA forms maintained on the PEC website will contain links to the clinical rationale on the PEC website. The Committee also decided that it would review and approve changes to the clinical rationale statements on the PEC website on an ongoing basis. The Committee reviewed and revised the clinical rationale statements for each of the drugs subject to prior authorization. The information on the PEC website will be updated to reflect these changes.

D. *Combination antifungal therapy for onychomycosis* – Prescription data from one MCSC indicated that only 9 patients received concurrent therapy with ciclopirox and a systemic antifungal during the 21-month time period from Jan 2000 to Sep 2001. The Committee concluded that the incidence of concomitant use is too low to warrant changing PA criteria for the antifungals for onychomycosis.

E. *Status of the PA for sildenafil (Viagra) in the NMOP and retail network* –MAJ Bellemin presented data from the NMOP assessing the potential impact of removing the sildenafil PA. He reported that the cost avoidance attributable to the PA for sildenafil in the NMOP over the 1-year time period April 2000 to March 2001 was about $14.00 per prescription using the same

model routinely used to monitor cost avoidance from the NMOP PA program. He recommended that the PA for sildenafil be continued.

Bill Hudson (Humana) also recommended that the sildenafil PA be continued. He presented data concerning the impact of the prior authorization for sildenafil in the TRICARE regions managed by Humana Military Healthcare Services (HMHS).

HMHS has required prior authorization for sildenafil in Regions 3/4 since mid June of 1998. Upon implementation of the PA requirement, utilization declined from over 1200 prescriptions per month to approximately 200 scripts per month. During 2000 through March 2001, utilization and prior authorization requests leveled off at approximately 500 scripts and 100 requests per month. Upon implementation of the TRICARE Senior Pharmacy program in April 2001, utilization approximately doubled, but the rate of denials remained constant at about 20%.

A distinctly different pattern is seen in Regions 2/5, which did not require prior authorization for sildenafil prior to April 2001. HMHS acquired the contract to manage these regions in June 2001. Sildenafil utilization was two to three times greater in Regions 2/5 than in Regions 3/4, even though the population of Regions 2/5 is about 20% smaller than Regions 3/4. During this time, Regions 3/4 had about 900 fewer claims per month than Regions 2/5 even though only about 30 requests for sildenafil were denied each month. The differences between Regions 3/4 and 2/5 in sildenafil utilization support the existence of a "sentinel effect" due to the presence of the PA program in Regions 3/4.

The PA may also enhance patient safety by assessing whether patients are currently receiving nitrates. The interaction between sildenafil and nitrates is one of the drug interactions most commonly detected by PDTS.

The Committee decided not to change the sildenafil PA in the NMOP or retail network.

11. **CLARIFICATION OF GROWTH HORMONE ON NMOP COVERED INJECTABLES LIST** – The Committee clarified the listing for somatropin, a human growth hormone, on the NMOP Covered Injectables list to include all of the brand names for this product. MAJ Mickey Bellemin confirmed that the NMOP is filling prescriptions for all brands of somatropin.

12. **CLARIFICATION OF HUMAN CHORIONIC GONADOTROPIN (HCG) PRODUCTS ON NMOP COVERED INJECTABLES LIST** – HCG is currently on the NMOP Covered Injectables List as "Human Chorionic Gonadotropin injection." The Committee added the recombinant HCG product Ovidrel (choriogonadotropin alfa) to the NMOP Covered Injectables List.

13. **ACCUTANE QUANTITY LIMIT** – Mark Petruzzi confirmed that the NMOP is complying with new FDA requirements for dispensing of Accutane, including limiting dispensing to a months supply and requiring a new prescription bearing a special sticker (which certifies that female patients have a negative pregnancy test and have received counseling on pregnancy prevention) prior to dispensing each months supply.

14. SUBCOMMITTEE REPORT: PROVISION OF INJECTABLE DRUGS IN THE NMOP OR RETAIL NETWORK PHARMACIES – LtCol (select) George Jones reported on the work of the subcommittee regarding provision of injectable drugs in the NMOP and retail network pharmacies. The subcommittee's goal was to optimize patient access, outcome, and satisfaction balanced with safety and cost efficiency. A guiding principle was that legislation or policy should not take the place of clinical judgment.

The subcommittee analyzed data from PDTS for MTFs, retail network pharmacies, and the NMOP to determine what injectable medications are being filled in each point of service. The subcommittee discussed the trend in the civilian sector to move high cost injectable drugs that were historically provided through provider offices into pharmacy distribution systems in an attempt to attain more control and information about injectable use and decrease costs through volume purchasing strategies.

LtCol (select) Jones commented that the subcommittee had not found any civilian plan that had a usable method of categorizing drugs into those that could be self-administered vs. those that should only be provided through provider offices. Plans differed drastically on what injectable drugs were covered as part of the pharmacy benefit, ranging from insulin and allergy kits only to an extensive list (basically everything except investigational drugs). Many plans have a positive list of drugs that are provided through the pharmacy benefit. Most plans have a system to handle exceptions and special needs. An industry report highlighted one plan that "optimized" distribution of injectables by directing patients to use mail order as their primary source for chronically used injectables.

The subcommittee made preliminary recommendations:

- Continue to provide injectables through the pharmacy benefit in the current manner. No significant misadventures or problems have been reported.
- Expand the number of injectables available through the NMOP. MAJ Bellemin and Mark Petruzzi (Merck-Medco) reported that the subcommittee would review Merck-Medco standard formulary planning list of injectable products as to what is usually covered. The subcommittee will review for next meeting and make specific recommendations. Mark Petruzzi noted that the idea of providing injectables to provider offices is something that Merck Medco is looking at for its commercial clients.
- MTFs continue to meet the needs of their patients through formulary addition or special purchases of injectable products.

15. CONTROLLED DISTRIBUTION OF DOFETILIDE (TIKOSYN) – Because of specialized educational requirements mandated by the FDA, dofetilide is only available for outpatient use through Stadtlander's Pharmacy/CVS Procare (which is a non-network pharmacy for DoD beneficiaries). LCDR Ted Briski reported that a plan has been worked out between Pfizer and DSCP to establish a centralized policy and financing procedure that should allow the drug to be obtained for DoD patients at federal pricing and prevent DoD patients from potentially having to pay the copay for a non-network pharmacy. Members commented that more drugs requiring controlled distribution systems are being approved and that similar issues are likely to continue to arise.

16. CONTROLLED DISTRIBUTION OF PEGINTERFERON ALFA 2B (PEG-INTRON; SCHERING) – Schering has instituted a special-distribution process for PEG-Intron due to concerns that unregulated distribution of the product could lead to shortages. Patients must begin the entire course of therapy again if it is interrupted.

Patients using retail network pharmacies or the NMOP will use the same process as Schering's commercial customers. Patients will call 888-437-2608 to self-enroll into the PEG-Intron Access Assurance program and receive an identification number. Patients will supply the identification number to the pharmacy along with their prescription or refill request. The pharmacy will place an order through its usual wholesaler, using the patient's ID number. The wholesaler will ship the product to the pharmacy to arrive within 5 days.

Patients using MTF pharmacies will not have to supply an identification number. MTF pharmacies will input the prescription into CHCS. The PDTS Customer Service Support Center will generate a weekly report of DoD patients newly started on PEG-Intron (using masked patient identifiers) and provide this to the PEG-Intron Access Assurance program. Schering will internally assign an ID number. No order authorization will be required. Schering is in the process of working out details of the program. Schering expects to submit a Memorandum of Understanding to DoD for approval before the end of the year.

17. 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, 13 February 2002. All agenda items should be submitted to the co-chairs no later than 11 January 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**
Cefditoren pivoxil tablets (Spectracef; TAP)	29 Aug 01; third generation cephalosporin for treatment of acute exacerbations of chronic bronchitis, pharyngitis, tonsillitis, and uncomplicated skin and skin structure infections	Added to the NMOP Formulary	**Quantity Limits** 10 days supply (40 tabs) per 30 days in NMOP and retail network **Rationale for Quantity Limits:** Spectracef is **only** indicated for acute therapy. Pivalate-containing compounds have caused clinical carnitine deficiency when used over a period of months. The effect of repeat short-term courses on carnitine levels is unknown. **Prior Authorization:** No	Not added to the BCF **Similar BCF Drugs:** Amoxicillin/ clavulanic acid oral; cephalexin oral (first generation cephalosporin)
Darbepoetin alfa for injection (Aranesp; Amgen)	17 Sep 01; erythropoietin analog for treating the anemia of chronic renal failure in dialysis and non-dialysis patients; administered every 1-2 weeks by IV or SQ injection	Added to the NMOP Formulary **Note**: Erythropoietin products (Epogen, Procrit) are currently on NMOP Covered Injectables List; darbepoetin alfa may be self-administered	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **Similar BCF Drugs:** none
Tramadol + acetaminophen tablets (Ultracet; Johnson & Johnson)	15 Aug 01; short-term (5 days or less) management of acute pain	Added to the NMOP Formulary **Note**: Although Ultracet is only indicated for short-term management of acute pain, both tramadol and acetaminophen are used on a longer-term basis; in addition, excluding the product from the NMOP Formulary would further delay therapy in the unlikely event that patients submit prescriptions for short-term therapy to the NMOP.	**Quantity Limits** 240 tablets per 30 days, 720 tablets per 90 days **Rationale for Quantity Limits:** Maximum daily quantity established by labeling as 8 tabs per day; consistent with existing quantity limits for tramadol **Prior Authorization** No	Not added to the BCF **Similar BCF Drugs:** multiple analgesics; tramadol is not on the BCF
Mixed salts of a single-entity amphetamine product, immediate/ delayed release (Adderall XR; Shire)	18 Oct 01; once daily treatment of attention deficit/hyperactivity disorder	Added to the NMOP Formulary	**Quantity Limits** NMOP: General rule for Schedule II controlled substances for treatment of ADHD applies (90 days supply; no refills) **Prior Authorization** No	Not added to the BCF **Similar BCF Drugs:** Methylphenidate oral (includes Concerta, but does not include Metadate CD)

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**
Ribavirin capsules (Rebetol; Schering-Plough)	26 July 01; anti-viral nucleoside analog capsules previously only available as a component of the combination product Rebetron, now available as a separate product indicated for combination use with interferon alfa 2b (Intron A) in chronic hepatitis C	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **Similar BCF Drugs:** none
Albuterol solution for inhalation - 0.63 mg/3 mL, 1.25 mg/3 mL (AccuNeb; Dey)	01 May 01; pre-mixed, pre-measured reduced dosages of albuterol inhalation solution for children with asthma aged 2-12	Already included on NMOP Formulary as new formulation of existing product	**Quantity Limits** 8 boxes of 25 per 30 days (200 unit doses); 22 boxes of 25 per 90 days (550 unit doses) **Rationale for Quantity Limits:** Consistent with existing quantity limits for nebulization solutions; sufficient to provide 6 treatments per day **Prior Authorization** No	Current BCF listing for albuterol solution for inhalation clarified to not include AccuNeb **Similar BCF Drugs:** albuterol solution for inhalation; albuterol oral inhaler
Comments about AccuNeb: The Council voted to exclude the new concentrations from the existing BCF listing for albuterol solution for inhalation because it seems doubtful that the incremental benefit will exceed the incremental cost. The Council also had concerns about the potential for medication errors (underdosing) if all MTFs are required to have all three strengths on their formularies. Council members noted that because the lower vital capacity of pediatric patients decreases total drug exposure, overdosing is not typically a problem with nebulized albuterol. If lower concentrations are desired, these may be easily attained with existing products.				
Amoxicillin/ Clavulanate Potassium Powder for Oral Suspension (Augmentin ES-600; Glaxo SmithKline)	22 Jun 01; Pediatric suspension of amoxicillin/clavulanate with double the previous concentration of amoxicillin, same clavulanate concentration; indicated for the treatment of pediatric patients with recurrent or persistent acute otitis media.	Already included on NMOP Formulary as new formulation of existing product	**Quantity Limits** General rule applies **Prior Authorization** No	Current BCF listing for amoxicillin/ clavulanic acid oral will include this new formulation **Similar BCF Drugs:** amoxicillin/ clavulanic acid oral
Comments about Augmentin ES-600: The Council noted that the cost per course of therapy with Augmentin ES-600 oral suspension appears to be comparable to giving standard concentration Augmentin plus an dose of amoxicillin suspension to provide the same amounts of amoxicillin and clavulanic acid. Other oral dosage forms with double concentrations of amoxicillin are already available and are also included in the BCF listing for amoxicillin clavulanic acid oral.				
Tenofovir disoproxil fumarate (Viread; Gilead Sciences)	26 Oct 01; in combination with other antiretroviral medications for the treatment of HIV infection	Already included on NMOP Formulary following precedent for HIV drugs. Confirmed by the Committee	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **Similar BCF Drugs:** None

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) Tretinoin cream, 0.025% and 0.05% [excludes products only indicated for wrinkles (e.g., Renova)]
      2) Diazepam 5 mg oral tablets
      3) Clonazepam 0.5 mg oral tablets
   B. *Deletions from the BCF*
      1) Cromolyn sodium oral inhaler
      2) Cromolyn sodium solution for inhalation
      3) Haloperidol oral
   C. *Changes and clarifications to the BCF*
      1) The current BCF listing for albuterol solution for inhalation was clarified to exclude the 0.63-mg/3 mL and 1.25 mg/3 mL strengths (AccuNeb)
      2) The current BCF listing for amoxicillin/clavulanic acid oral will include Augmentin ES-600 oral suspension
2. **NMOP FORMULARY CHANGES**
   A. *Additions to the NMOP Formulary* (See Appendix A for details)
      1) Rabeprazole oral (interim decision effective 1 Oct 2001)
      2) Pantoprazole oral (interim decision effective 1 Oct 2001)
      3) Lansoprazole oral (as of 15 Nov 2001)
      4) Choriogonadotropin alfa (Ovidrel) for injection – added to NMOP Covered Injectables List
      5) Ceftidoren pivoxil tablets (Spectracef; TAP) – quantity limits apply, see below
      6) Darbepoetin alfa for injection (Aranesp; Amgen) – added to NMOP Covered Injectables List
      7) Tramadol/acetaminophen 37.5 / 325 mg tablets (Ultracet; Johnson & Johnson) – quantity limits apply, see below
      8) Mixed salts of a single-entity amphetamine product, immediate/delayed release (Adderall XR; Shire)
      9) Ribavirin capsules (Rebetol; Schering-Plough)
      10) Tenofovir disoproxil fumarate (Viread; Gilead Sciences)
   B. *Exclusions from the NMOP Formulary*
      1) Lansoprazole oral (interim decision effective 1 Oct 2001; lansoprazole was added to the NMOP Formulary as of 15 Nov 2001)
      2) Esomeprazole oral (interim decision effective 1 Oct 2001; esomeprazole remains excluded from NMOP Formulary)

C. Clarifications to the NMOP Formulary

1) Listing for somatropin (human growth hormone) on NMOP Covered Injectable List clarified to list all of the brand names for this product

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

A. Quantity limit for cefditoren pivoxil tablets: 10 days supply (40 tablets) per 30 days in NMOP and retail network

B. Quantity limit for tramadol/acetaminophen 37.5/325 mg tablets: 240 tablets per 30 days; 720 tablets per 90 days

C. Albuterol solution for inhalation – 0.63 mg/3 mL, 1.25 mg/3 mL: 8 boxes of 25 per 30 days (200 unit doses); 22 boxes of 25 per 90 days (550 unit doses)

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

Department of Defense
Pharmacoeconomic Center

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MCCS-GPE **14 November 2001**

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 14 November 2001 at the Uniformed Services University of the Health Sciences. The DoD P&T Executive Council is responsible for performing certain inherently governmental functions relevant to the DoD pharmacy benefits program. The Council focuses primarily on issues related to the Basic Core Formulary (BCF), national pharmaceutical contracts, and blanket purchase agreements. The DoD P&T Executive Council is comprised of federal employees who are members of the DoD P&T Committee.

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 Bill Sykora, MC	Air Force
LtCol (select) George Jones, BSC	Air Force
CAPT (select) Matt Nutaitis, MC	Navy
CDR Kevin Cook, MSC	Navy
COL Mike Heath, MS (representing MAJ Brett Kelly)	Army
COL Rosa Stith, MC	Army
LTC (P) Joel Schmidt, MC	Army
CAPT Chuck Bruner	Coast Guard
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
LTC Mike Kieffer, MS	Joint Readiness Clinical Advisory Board

MEMBERS ABSENT

Dick Rooney	Department of Veterans Affairs

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
COL Ardis Meier, BSC	Air Force Pharmacy Consultant
CAPT Betsy Nolan, MSC	Navy Pharmacy Specialty Leader
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
LTC Deborah Bostock, MC	Air Force
CDR Denise Graham, MSC	DoD Pharmacoeconomic Center
LCDR Ted Briski, MSC	DoD Pharmacoeconomic Center
MAJ Cheryl Filby, MS	Defense Supply Center Philadelphia
MAJ Maria Ionescu	Pharmacy Benefits Division, TMA
MAJ Barb Roach, MC (by teleconference)	DoD Pharmacoeconomic Center
Howard Altschwager	Deputy General Counsel, TMA
Dave Bretzke	DoD Pharmacoeconomic Center
Michael McGregory	Pharmacy Student, Butler University Pharm.D. Program
Shirif Mitry	Pharmacy Student, TMA
Shana Trice	DoD Pharmacoeconomic Center
Paul Vasquez	Defense Supply Center Philadelphia

3. REVIEW MINUTES OF LAST MEETING / ADMINISTRATIVE ISSUES

The Council approved the minutes of the last meeting with two corrections:

- The reference to seborrheic keratoses on Page 15 of the Aug 01 DoD P&T Executive Council minutes was changed to actinic keratoses.
- The prescription data in Table 2 on Page 3 of the Aug 01 DoD P&T Executive Council minutes are incorrect. The corrected table is shown below:

Table 2: Prescription fills for COX-2 Inhibitors and Traditional NSAIDs in the MHS, July 2001

	MTF prescriptions	MCSC retail network prescriptions	NMOP prescriptions	Total
COX-2 inhibitors	45,201 (15%)	40,106 (59%)	12,824 (74%)	98,131 (26%)
Traditional NSAIDs	252,134 (85%)	27,857 (41%)	4,480 (26%)	284,471 (74%)
Total	297,335	67,963	17,304	382,602

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4. ADVANCES IN MEDICAL PRACTICE (AMP) PROGRAM

According to prime vendor data, Military Treatment Facilities (MTFs) spent $46.5 million on AMP drugs in FY 2001. Prime vendor data are incomplete for 44 MTFs in the second half of FY 01, so MTFs actually spent more than $46.5 million on AMP drugs during FY 01.

5. SUBCOMMITTEE REPORT: OBTAINING INPUT FROM PROVIDERS

COL Downs reported how the VA uses the Medical Advisory Panel (MAP) and the regionally based formulary management process in the 22 Veterans Integrated Service Networks (VISNs) to systematically obtain input from providers on formulary and contracting issues. The Council noted that most TRICARE regions have not established a regional formulary management process. LCDR Briski reported a lack of consensus among pharmacy officers regarding methods to obtain prescriber input. Some pharmacy officers favor communicating through lead agents, while others favor military service lines of communication.

LtCol (select) George Jones noted that actions of the DoD P&T Committee are a standing agenda item for his local P&T committee, which prompts input and communication. He suggested that MTF P&T Committees should routinely include DoD P&T Committee actions on their meeting agendas. He also noted that the PEC website provides access to DoD P&T Committee documents. (The PEC website is available at www.pec.ha.osd.mil.)

The Council decided to obtain prescriber input primarily by having the PEC communicate with the chairs of MTF and/or regional P&T committees and MTF pharmacy chiefs. The Council did not reach a definitive conclusion regarding the process that will be used to accomplish this type of communication. However, there was support voiced for including lead agent pharmacists and medical directors as integral parts of the process. The PEC agreed to present various process options at the next meeting.

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

A. *Contract awards, renewals, and terminations*

- As of November 2001, 54 joint VA/DoD and 3 DoD-only contracts for drugs or pharmaceutical supplies are in effect. A joint VA/DoD returned goods contract is also in effect. Information on national pharmaceutical contracts, including NDC numbers and prices, is available on the DSCP website (www.dmmonline.com).
- Contracts for terazosin, acyclovir, hydroxyurea, pentoxifylline, rifampin, sucralfate, nortriptyline, prazosin, diltiazem XR, ranitidine, insulin, verapamil, and albuterol inhalers were renewed.
- The cimetidine contract was extended until May 02.
- Contracts for cerivastatin, amoxicillin, azathioprine, and omeprazole were cancelled.
- New contracts were awarded for cyclobenzaprine tablets, isosorbide dinitrate tablets, loperamide capsules, methocarbamol tablets, verapamil immediate release tablets, and lactulose syrup.

B. *Financial impact of contracts* – COL Remund reported on the percent reduction in cost per unit for drugs covered by national pharmaceutical contracts (see Table 1).

Table 1: Percent Reduction in Cost per Unit for Drugs Covered by National Pharmaceutical Contracts*

Drug/Drug Class	% Reduction
Diltiazem extended release	48%
Lisinopril	45%
PPIs	36%
Non-sedating antihistamines	36%
Statins	31%
All contracts	33%

*From start dates of contracts to 30 Sep 2001

C. *Status of Contracting Initiative for Leutinizing Hormone Releasing Hormone (LHRH) agonists* – CAPT Torkildson reported that the joint VA/DoD contracting action to select a LHRH agonist for the Basic Core Formulary (BCF) (for the treatment of prostate cancer only) is awaiting completion of updates to the VA clinical review. The VA extended its contract for Zoladex until early 2002 in preparation for a joint VA/DoD contracting initiative. The DoD Blanket Purchase Agreements (BPAs) for Lupron and Zoladex remain in place. The BPA for Zoladex has been modified since the last meeting to remove the market share requirement and to extend the expiration date of the BPA until 30 April 2002. The Lupron BPA has also been modified to maintain the current price until 30 April 2002.

D. *Non-sedating antihistamine contract* – The market share for fexofenadine (as a percent of all prescriptions for non-sedating antihistamines dispensed at MTF pharmacies) increased from 50% prior to the contract to approximately 89% by the end of October 2001. The prescription market shares for fexofenadine and loratadine continue to remain stable in the retail pharmacy networks and the National Mail Order Pharmacy (NMOP), indicating that MTFs are maximizing the use of fexofenadine without shifting loratadine prescriptions into the retail pharmacy network or NMOP. The average cost per non-sedating antihistamine tablet/capsule purchased by MTFs dropped by 36%, from $0.87 (pre-contract) to $0.56 (as of Sep 2001).

E. *Statin Contract* – The Council considered two options regarding the renewal of the simvastatin contract:

Option 1: Renew the simvastatin contract for the final option year (February 2002 to February 2003). The statin class remains "closed" on the BCF. Simvastatin is the only statin on MTF and NMOP formularies.

Option 2: Do not renew the simvastatin contract. The statin class would be "open" on the BCF. MTFs may have additional statins on formulary. DoD P&T Committee decides which statins are on the NMOP formulary.

The Council assessed the relative safety/tolerability of statins; effectiveness in reducing LDL-cholesterol; evidence of effect on cardiovascular morbidity and mortality; ability of simvastatin to meet the clinical needs of the DoD beneficiary population; current statin

costs; likelihood of future price reductions for simvastatin, input from providers; and potential collaboration with the VA on the statin class in the future.

The Council concluded that:

- Simvastatin has a well-established safety and tolerability profile.
- Simvastatin is proven to reduce cardiovascular morbidity and mortality.
- Simvastatin is currently used by > 95% of statin patients at MTFs.
- Non-contracted statins can be provided through the special order process for patients who need them.
- Simvastatin is more cost-effective than other statins in treating patients to LDL goal.
- The cost per dose of statin therapy has decreased by 31% at MTF pharmacies in the first two years of the statin contract. Additional reductions in the cost per dose are more likely to occur if the contract is renewed than if it is not renewed.
- The VA strategy for managing statins is linked to renewal of the DoD statin contract.
- Contract renewal will facilitate joint management of statins by DoD and VA.

The Council decided to advise DSCP to renew the contract for simvastatin.

F. *Status of contracting initiative for nasal corticosteroid inhalers* –The Council reviewed an updated analysis of aqueous nasal corticosteroid dosing frequency and input from providers to assess whether or not flunisolide should be included in a solicitation for a closed class contract.

- An analysis of MTF prescription data from Jun 00 to May 01 showed the following percentages of patients who were treated with a single daily dose of an aqueous nasal corticosteroid:

fluticasone	93.7%
mometasone	93.7%
beclomethasone 84mcg	91.9%
triamcinolone	85.5%
budesonide	60.0%
flunisolide	27.2%

- DoD providers report a higher rate of burning and stinging with flunisolide than with other nasal corticosteroid products.

The Council concluded that flunisolide should not be included in the solicitation because it is dosed more than once daily much more frequently than other products and because providers have reported tolerability problems. The Council concluded that budesonide should not be included in the solicitation because it is dosed more than once daily much more frequently than other products. The Council also recommended that:

- The contract should not apply to use of aqueous nasal steroids in patients under 6 years of age. While it is not known whether the nasal corticosteroids differ significantly in their potential to affect the growth and development of pediatric patients, the Council prefers to allow MTFs to select an alternate agent for this patient

population if they so desire. The PEC estimates that less than 4% of all aqueous nasal steroid inhaler prescriptions are for patients who are under 6 years of age, so exclusion of this patient population will not have a negative impact on the contract.

- The contract should specify that all new patient starts must use the contracted agent, but should not dictate that existing patients be switched to the contracted agent.

The Council reiterated its support for a joint VA/DoD solicitation if agreement can be reached on the products that are included in the solicitation. If agreement cannot be reached, the Council recommends that DoD pursue its own contract.

G. *Potential contracting initiative for carbamazepine* – Multiple AB-rated generic products are available for commonly used strengths of carbamazepine. MTF usage of carbamazepine has declined about 20% over the past two years to a current usage rate of 700,000 tablets/month. MTFs spent about $1.5 million on carbamazepine during FY 01 ($1.4 million for the brand name product (Tegretol) and $0.1 million for generic products). The average cost is currently $0.22/tablet for Tegretol and $0.05/tablet for generic carbamazepine.

Generic versions of carbamazepine currently account for about 20% of total carbamazepine usage at MTFs (up from 5% two years ago). In light of the large cost difference between the brand and generic versions of carbamazepine, the Council asked the PEC to investigate why the usage of the brand name drug continues to predominate at MTFs.

H. *Potential contracting initiative for triptans* – In the absence of information that negates concerns about variability in patient response, the Council is unwilling to support a closed class contract for a single oral triptan. The Council asked the PEC to continue to explore potential contracting initiatives for this drug class.

I. *Potential contracting initiative for angiotensin receptor blockers (ARBs)* – MTF utilization and expenditures for the ARBs are rising, and clinical information concerning these agents is evolving. The PEC is collaborating with the VA Pharmacy Benefits Management Strategic Healthcare Group (VA PBM) on a class review of the ARBs. The Council asked the PEC to continue to work with the VA to complete the class review and explore the feasibility of contracting initiatives in this drug class.

J. *Contracting initiative for fluoroquinolones* – Independent class reviews completed by the VA PBM and the PEC concluded that gatifloxacin (Tequin) and levofloxacin (Levaquin) offer advantages over the other fluoroquinolones in safety and tolerability (side effect and drug interaction profiles), expanded gram-positive spectrum of activity, and once daily dosing. Both reviews concluded that levofloxacin and gatifloxacin are the only two fluoroquinolones that are therapeutically interchangeable and clinically acceptable as a "workhorse" oral fluoroquinolone. Levofloxacin is currently on the BCF in accordance with a BPA.

Ciprofloxacin is dosed twice daily, has poor coverage for *S. pneumoniae*, and has several clinically significant drug interactions. The Council concluded that ciprofloxacin is not therapeutically interchangeable with gatifloxacin or levofloxacin. The Council noted that

ciprofloxacin is the only fluoroquinolone currently approved for post-exposure prophylaxis of anthrax, but the proposed contract initiative would not affect the availability of usage of ciprofloxacin for anthrax exposures.

The DoD P&T Executive Council agreed to support a contracting initiative to choose a workhorse oral fluoroquinolone for the BCF.

7. MTF REQUESTS FOR BCF CHANGES

A. *Request to remove cromolyn sodium oral inhaler and solution for inhalation from the BCF* –An Army pharmacist provided the following rationale for the request:

> Cromolyn is relatively infrequently used in clinical practice. Cromolyn is a weak anti-inflammatory agent and is rarely prescribed. Inhaled steroids are used almost exclusively for this indication and are now acceptable in patients <2years of age with use of a spacer mask.

The mast cell stabilizers (cromolyn and nedocromil) produce only minor side effects (nasal congestion, cough, sneezing, dry throat). Nedocromil has an unpleasant taste. Mild-persistent asthma can be controlled with cromolyn in approximately 60 to 75% of patients, but 4 to 6 weeks of usage four times a day may be needed to attain maximum benefit. The mast cell stabilizers are not as effective as the inhaled corticosteroids, which are the agents of choice for long-term control of persistent asthma.

The PEC requested provider input on this issue and received 129 responses: 70 favoring removal from the BCF; 42 against removal from the BCF; 13 unsure; and 4 wanted to remove the MDI, but keep the nebulizer solution. Providers made several key points:

- Keeping cromolyn on the BCF may promote less effective, outdated therapy. Removing it from the BCF may encourage providers to more appropriately treat persistent asthma with inhaled corticosteroids.
- Despite parental concerns, studies reporting growth reduction with inhaled corticosteroids do not offer sufficient justification for avoiding the use of inhaled corticosteroids in children with asthma.
- Data suggest that delays in initiating maintenance therapy with inhaled corticosteroids result in less recovery of lung function in children with asthma.
- The best evidence for use of cromolyn is for people whose asthma symptoms are solely induced by exercise and who do not tolerate a long-acting beta agonist like salmeterol.

Prescriptions for cromolyn MDIs at MTFs declined by 52% over the past year, from 3265 prescriptions in Sep 2000 to 1562 prescriptions in Sep 2001. Prescriptions for cromolyn nebulizer solution declined by 55%, from 957 Rxs in Sep 2000 to 434 in Sep 2001.

The Council removed cromolyn sodium oral inhaler and solution for inhalation from the BCF. MTFs can decide whether or not to keep either or both products on their local formularies.

B. *Request to remove oral haloperidol from the BCF* – An Army pharmacist based this request on the relatively infrequent usage of haloperidol at his MTF.

Haloperidol is a potent antipsychotic with a high propensity to cause adverse effects. MTFs currently fill about 500 haloperidol prescriptions per month. Newer agents such as risperidone, olanzapine, and quetiapine are used more frequently than haloperidol. Primary care providers in the outpatient setting do not commonly prescribe antipsychotics. The Council removed oral haloperidol from the BCF. MTFs can decide whether or not to keep oral haloperidol on their local formularies.

C. *Request to add a no to extremely low androgen oral contraceptive to the BCF* – An Army pharmacist originally requested the addition of Desogen, a monophasic oral contraceptive (OCP) to the BCF. The request was subsequently clarified to be for the addition of a "3rd generation" monophasic OCP classified as having no to low androgenic side effects and 35 mcg of ethinyl estradiol. These OCPs contain the progestin desogestrel (Desogen, Ortho-Cept, Apri) or norgestimate (Ortho-Cyclen).

The purported advantages of OCPs with no to low androgenic effects are lower incidences of weight gain, edema, bloating hirsutism and acne. MAJ Barb Roach reported that she could not find empirical evidence that OCPs differ significantly in androgenic side effects. Head-to-head trials are not available. Most reviewers acknowledge that there is no evidence of significant differences in side effects or efficacy for any of the OCPs, regardless of the progestin contained in the pill or their classification as mono-, bi-, tri-, or estro-phasic products. However, the same reviewers then go on to discuss differences in androgenic side effects with different progestins (apparently based primarily on *in vitro* characteristics of the progestins). A number of providers commented on the propensity for misconception in this therapeutic category.

All OCPs are associated with an increased risk of venous thromboembolism. Some studies suggest an increased potential for venous thromboembolism with the 3rd generation OCPs compared to other OCPs, but the evidence is inconclusive.

The 3rd generation OCPs cost from $10.20 to $15.28 per cycle—much more than most other OCPs. The Council decided not to add a 3rd generation OCP to the BCF because there is insufficient evidence that an incremental clinical benefit exists that would justify the incremental cost.

8. FORMULARY STATUS OF TRETINOIN

Tretinoin cream is indicated for the treatment of acne, and is also commonly used for the treatment of various skin cancers, precancerous conditions (e.g., actinic keratoses), and other dermatological conditions. Tretinoin products are also used for cosmetic treatment of photoaged skin (wrinkles and liver spots). One brand of tretinoin cream, Renova, is specifically indicated for mitigation of fine wrinkles, mottled hyperpigmentation and tactile skin roughness in patients who use comprehensive skin care and sunlight avoidance programs.

Topical retinoids are first line agents for acne. More than 95% of MTFs already have tretinoin cream on formulary. The Council decided to add tretinoin cream 0.025% and 0.05% to the BCF, but excluded products specifically indicated for wrinkles only (e.g., Renova). The Council noted that MTFs may adopt guidelines or retain existing guidelines designed to prevent usage of tretinoin products for cosmetic treatment of photoaged skin.

The NMOP statement of work does not allow tretinoin prescriptions to be filled for patients over the age of 35. The rule exists only in the NMOP statement of work—not in the Code of Federal Regulations or TRICARE policy. PDTS data show that tretinoin prescriptions are routinely filled in MTF and retail pharmacies for patients over the age of 35. The Council considered a proposal to remove the NMOP age restriction so that tretinoin would be more uniformly available to patients across all points of service. Some attendees expressed concern about taking an action that would require modification of the NMOP contract. After extensive discussion, the vote to remove the NMOP age restriction on tretinoin ended in a tie. The age restrictions on tretinoin remain in the NMOP. .

9. REVIEW OF ANXIOLYTICS FOR THE BCF

CAPT Torkildson reported on the PEC review of drugs for the treatment of anxiety disorders: generalized anxiety disorder (GAD), panic disorder/agoraphobia, acute/post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), specific phobia, and social phobia. These six conditions share a common dimension of poor response to stress leading to frequent and intense episodes of negative affect. This dimension is shared with depressive disorders, and is primarily responsible for the observed comorbidity among the anxiety disorders and between these disorders and depression. Each disorder also contains a unique component that distinguishes it from the others, with the possible exception of GAD.

Pharmacotherapy for anxiety disorders includes serotonin reuptake inhibitors [selective serotonin reuptake inhibitors (SSRIs) and venlafaxine]; benzodiazepines; buspirone; tricyclic antidepressants (TCAs); imipramine; clomipramine; trazodone; and nefazodone. Of these, buspirone, imipramine, trazodone, and four SSRIs are on the BCF.

Serotonin Reuptake Inhibitors – This classification includes the SSRIs and venlafaxine. There is growing support for using this group of drugs as first line therapy for many of the anxiety disorders. SSRIs are now considered the treatment of choice for panic disorder and post-traumatic stress disorder, and as first choice in conjunction with psychotherapy for OCD, specific phobia, and social phobia. Usage of SSRIs for treatment of GAD is increasing. Despite differences in FDA-approved indications, the SSRIs appear similar in safety and efficacy for these conditions. There are already four SSRIs (citalopram, fluoxetine, paroxetine, sertraline) on the BCF.

Venlafaxine inhibits both serotonin and norepinephrine reuptake (similar to TCAs). It was approved by the FDA for depression in 1993, and for GAD in 1999. It has been shown to be effective for GAD with and without coexisting depression. Venlafaxine appears to have a rapid onset of action with a safety profile similar to the SSRIs. Venlafaxine appears to be less costly on a cost per day basis than fluoxetine, paroxetine, or sertraline. It is currently on approximately 88% of MTF formularies, but it is not on the BCF.

The Council decided not to change the SSRIs on the BCF, but instructed the PEC to investigate the potential for addition of venlafaxine extended-release to the BCF as a cost-effective alternative to the SSRIs for the treatment of anxiety disorders.

Benzodiazepines – Benzodiazepines are effective in treating anxiety disorders, including GAD, panic disorder, and social anxiety disorder. The long-term use of benzodiazepines for anxiety disorders is controversial. All benzodiazepines share a risk of sedation, motor vehicle accidents, industrial accidents, and dependence. Rebound anxiety occurs in approximately 15% of patients upon discontinuation. The benzodiazepines are Pregnancy Category D due to the risk of cleft lip/palate. There are currently no benzodiazepines on the BCF.

All benzodiazepines used for treatment of anxiety disorders are available as generics. All strengths of these benzodiazepines are available for less than $0.10 per tablet or capsule. As Schedule IV medications, the administrative burden associated with stocking and record keeping must be considered in adding any of them to the BCF.

Psychiatrists identified clonazepam as a drug that should be considered for the BCF because of a lower abuse potential and more utility in other conditions (e.g., some seizure disorders). Almost all MTFs (99%) are filling prescriptions for the 0.5 mg strength of clonazepam. Some MTFs appear to carry only the 0.5 mg strength.

According to the PEC Formulary database, 100% of facilities have diazepam on their local formulary. About 97% of prescriptions for oral diazepam tablets are for the 5 mg strength.

The Council decided to add clonazepam 0.5 mg and diazepam 5 mg to the BCF. MTFs may have other strengths or formulations of these medications on their formularies.

Buspirone – The utility of buspirone is limited primarily to treatment of GAD. Buspirone has a superior safety profile compared to the benzodiazepines, but a significantly slower onset of action. Many think buspirone is less efficacious than other agents, but under-dosing might be the problem. Buspirone is already on the BCF and MTF pharmacies dispensed nearly 6 million tablets in the first 9 months of FY 01. The Council agreed that buspirone should remain on the BCF.

Tricyclic Antidepressants – Imipramine is useful primarily in GAD. Clomipramine is used to treat OCD. The usefulness of these agents is limited by their side effect profile and potential for accidental or deliberate overdose. SSRIs are equally efficacious, safer, and much better tolerated. Imipramine is already on the BCF. There is no provider support for the addition of clomipramine. The Council made no changes in this drug class.

Trazodone – Trazodone is a heterocyclic antidepressant. Anxiolytic use has been confined primarily to GAD. Although trazodone has no significant safety, tolerability, or efficacy advantages over other active agents, it is relatively inexpensive. Trazodone also has some utility in treating insomnia resulting from SSRI therapy. Trazodone is already on the BCF. The Council made no change to the formulary status of trazodone.

Nefazodone – Nefazodone is an antidepressant with a unique mechanism of action. It was FDA-approved in 1994 for treatment of depression, but is used off-label to treat panic disorder, PTSD, and social phobia. The major advantage of nefazodone is its somewhat superior safety profile, but the daily cost per day of therapy is $1.06 to $3.18. Nefazodone is not on the BCF. Providers expressed no interest in the addition of nefazodone to the BCF and usage in the Military Health System (MHS) is relatively low. The Council made no change in the formulary status of nefazodone.

10. EVALUATION OF THE CLOPIDOGREL IN UNSTABLE ANGINA TO PREVENT RECURRENT EVENTS (CURE) TRIAL

The CURE trial randomized approximately 12,500 patients (500 patients in the U.S. arm) with unstable angina and non-ST-segment elevation myocardial infarction (MI) presenting within 24 hours of symptom onset to clopidogrel (300 mg load, followed by 75 mg daily, plus aspirin in doses ranging from 75 to 325 mg daily) or aspirin plus placebo. Patients were treated for 3 to 12 months (average of 9 months).

The primary composite outcome of non-fatal MI, stroke, or death due to cardiovascular causes occurred in 9.3% of patients receiving clopidogrel plus aspirin compared to 11.4% of patients receiving aspirin plus placebo. This equates to a relative risk of 0.80 (95% CI 0.72-0.90, $p<0.001$), or a 20% relative risk reduction. The absolute risk reduction was 2.1%, which yields a number needed to treat of 47. The addition of clopidogrel to aspirin appeared to provide both an early (within 2 hours) and sustained benefit.

If 100 patients analogous to those obtaining benefit in the CURE trial were treated for a 9 month period with clopidogrel plus aspirin and a similar group of 100 patients were treated with aspirin only, drug costs for the clopidogrel plus aspirin group would be about $50,220 ($1.86 per patient per day) compared to about $270 ($0.01 per patient per day) for the aspirin only group. Given outcomes of the CURE trial, 9 patients (9.3%) in the clopidogrel plus aspirin group and 11 (11.4%) in the aspirin only group would be expected to experience the primary outcome of non-fatal MI, stroke, or death. Dividing the incremental cost of clopidogrel therapy ($50,220 - $270) by the number of averted events (2) results in an incremental cost of $25,000 per averted event.

The increased risk of bleeding in the clopidogrel plus aspirin group must also be considered. During the CURE trial, a significantly higher percentage of patients receiving clopidogrel plus aspirin experienced major bleeding compared to those receiving aspirin plus placebo (3.7% vs 2.7%, $p = 0.001$), a number needed to harm of 100. Thus, for every 100 patients treated with clopidogrel plus aspirin, one additional patient would be expected to have a major bleed compared to 100 patients receiving aspirin alone (or one major bleed per two events averted). Combination therapy also resulted in a significantly higher percentage of patients experiencing non-life threatening bleeding, minor bleeding, and bleeding requiring transfusion of $\geq$ 2 units of blood. 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).

The definitions used in the CURE trial for the various types of bleeding differ from widely accepted definitions used in the ACCP Consensus Conference on Antithrombotic Therapy guidelines published each year in CHEST (the “CHEST guidelines”) and the “Thrombolysis in Myocardial Infarction” (TIMI) trials. The variance in bleeding definitions raises the

concern that the risk of bleeding among patients receiving clopidogrel plus aspirin may have been even larger if the bleeding definitions in the CHEST guidelines and TIMI trials had been used.

The Council decided not to add clopidogrel to the BCF. The Council asked the PEC to request additional information from the manufacturer about the incidence of bleeding found in the CURE trial—ideally information about the bleeding rates using the definitions found in the CHEST guidelines and TIMI trials.

11. PROTON PUMP INHIBITORS

COL Remund reported on a significant shift in proton pump inhibitor (PPI) prescription market shares after omeprazole (Prilosec) was removed and rabeprazole (Aciphex) was added to the BCF on 1 October 2001. By the first week in November, rabeprazole accounted for 54% of MTF PPI prescription fills. The rapid switch to rabeprazole by MTF pharmacies essentially negated the effect of the huge increase in the price of omeprazole. The weighted average cost per unit for PPIs increased significantly during the first part of October, but trended back down to $1.08 per unit by the first week in November (just under the $1.09 cost per unit that existed prior to termination of the omeprazole contract).

12. COX-2 INHIBITORS

MTF prescription fills and expenditures for the COX-2 selective inhibitors (celecoxib and rofecoxib) leveled off over the past six months. Council members speculated that uncertainty about cardiovascular safety and the ability of these agents to significantly reduce the risk of GI events (especially in patients taking aspirin for cardiac prophylaxis) may have played a role.

13. ADJOURNMENT

The meeting adjourned at 1600 hours on 14 Nov 2001. The next meeting will be held at the Non-Commissioned Officers Club, Fort Sam Houston, TX starting at 0800 on 12 Feb 2002. All agenda items should be submitted to the co-chairs no later than 11 Jan 2002.

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

Department of Defense
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MCCS-GPE **16 AUGUST 2001**

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 16 August 2001, at the Non-Commissioned Officers Club, Ft. 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
LtCol (select) 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, MS	Army
CAPT Robert Rist	Coast Guard
LTC Mike Kieffer, MS	Joint Readiness Clinical Advisory Board
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia (DSCP)
William Hudson	Humana, Inc
Gene Lakey	TriWest
Trevor Rabie	Uniformed Services Family Health Plans (USFHP)

MEMBERS ABSENT

COL Rosa Stith, MC	Army
Dick Rooney	Department of Veterans Affairs
Ray Nan Berry	Health Net Federal Services
Ron McDonald	Sierra Military Health Services

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
COL Mike Heath, MS	Army Pharmacy Consultant; Chair, DoD Pharmacy Board of Directors
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
LtCol Gary Blamire, MSC	Lead Agent Office, Region 6
LTC Don De Groff, MS	DoD Pharmacoeconomic Center
LTC Doreen Lounsbery, MC	DoD Pharmacoeconomic Center
LtCol Ed Zastawny, BSC	DoD Pharmacoeconomic Center
LCDR Ted Briski, MSC	DoD Pharmacoeconomic Center
MAJ Cheryl Filby, MS	Defense Supply Center Philadelphia
MAJ Barbara Roach, MC	DoD Pharmacoeconomic Center
Capt Andrew Meadows, BSC	Baylor University Resident
SFC Augustin Serrano	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
David Bretzke	DoD Pharmacoeconomic Center
David Chicoine	Uniformed Services Family Health Plan
Eugene Moore	DoD Pharmacoeconomic Center
Mark Petruzzi	Merck-Medco
Carol Scott	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
Paul Vasquez	Defense Supply Center Philadelphia
Gina Wu	Merck-Medco

3. **REVIEW MINUTES OF LAST MEETING / ADMINISTRATIVE ISSUES** – The minutes from the last meeting erroneously listed Shannon Rogers as an employee of Merck-Medco. Ms. Rogers is an employee of Humana.

4. **UNIFORM FORMULARY**– COL Davies reported that a draft of the Uniform Formulary regulation is being staffed in TMA.

5. 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 the 6 new drugs listed below. See Appendix A for more information.

- Almotriptan 6.25- and 12.5-mg tablets (Axert; Pharmacia & Upjohn)
- Drospirenone 0.3 mg / ethinyl estradiol 30 mcg tablets (Yasmin; Berlex);
- Desogestrel/ethinyl estradiol tablet (Cyclessa; Organon)
- Valganciclovir tablets (Valcyte; Syntex)
- Albuterol sulfate 3 mg and ipratropium bromide 0.5 mg per 3 mL (DuoNeb Solution for Inhalation; Dey Labs)
- Insulin aspart injection (NovoLog; Novo Nordisk)

6. USAGE PATTERNS OF DRUGS FORMERLY ON NMOP PREFERRED DRUG PROGRAM – On 1 April 2001, Merck-Medco (the NMOP contractor) ceased making calls to physicians concerning all non-preferred/preferred drug pairs in the NMOP Preferred Drug Program except diltiazem. The committee was interested in seeing how discontinuation of the preferred drug program affected usage patterns of these drugs. Oxybutynin immediate release and Adalat CC experienced the largest drop in market share versus the non-preferred products. The market share changes for ranitidine, acyclovir, and generic NSAIDs were much smaller. Except for the antiviral drugs (acyclovir, famciclovir, valacyclovir), all the products experienced sharp increases in prescription volume because of the implementation of the TRICARE Senior Pharmacy Program.

7. PRIOR AUTHORIZATIONS

A. *Temporary lapse in the NMOP Prior Authorization Program* – Prior authorizations in the NMOP were temporarily suspended in April and early May due to sharp increases in workload associated with the expansion of the pharmacy benefit to all beneficiaries over 65 years of age. Table 1 shows when specific PAs were "turned off" in the NMOP. Initial implementation of the PA for ciclopirox topical solution (Penlac) was delayed to 10 May 2001.

Table 1: Temporary suspension of NMOP PAs due to the Apr 01 benefit change

Drug	"Turned off"	"Turned back on"
Antifungals for onychomycosis [itraconazole (Sporanox), terbinafine (Lamisil)]	10 April 01	1 May 01
Antifungals for onychomycosis [(ciclopirox top solution (Penlac)]	NA	10 May 01
COX-2 inhibitors [celecoxib (Celebrex), rofecoxib (Vioxx)]	14 April 01	30 April 01
Etanercept (Enbrel)	14 April 01	30 April 01
Sildenafil (Viagra)	10 April 01	10 May 01

B. *Cost avoidance from NMOP prior authorizations (PAs)* – Shana Trice (PEC) reported that cost avoidance analyses were not completed for this quarter due to the temporary suspension of the NMOP PA Program. Merck-Medco is now supplying data that identifies new and refill prescriptions, which should improve the accuracy of cost avoidance analyses.

C. *Utilization of the NMOP and retail network pharmacies for drugs subject to PA* – An analysis of the potential shift of patients with prescriptions for COX-2 inhibitors from the NMOP to the retail network is underway, using data from PDTS.

D. *Revision of NMOP PA forms* – Changes to clinical rationale language for the COX-2 inhibitors were delayed by the temporary suspension of the NMOP PA program. Further discussion with Merck-Medco is required to incorporate clinical rationale language for this drug class into the fax forms used by Merck-Medco. Changes to clinical rationale language for the antifungals for onychomycosis to reflect safety announcements by the Food and Drug Administration (FDA) concerning terbinafine and itraconazole are in progress.

E. *Status of the PA for sildenafil (Viagra) in the NMOP and retail network* – MAJ Bellemin commented that the sildenafil PA is responsible for the most patient complaints of all PAs in the NMOP. He suggested that quantity limits already in effect (6 tabs per 30 days for the retail network; 18 tabs per 90 days for the NMOP) might be sufficient to control over-utilization without a PA. The PA for sildenafil was established by a Health Affairs policy, so the PA cannot be discontinued unless the policy is changed. Other drugs similar to sildenafil may be on the market soon, which may provide an impetus to change the sildenafil policy. .

COL Davies commented that the information in the current sildenafil PA regarding drug interactions and contraindications has a questionable impact on prescribing, since the second most frequently reported potential drug-drug interaction in PDTS is concomitant sildenafil and nitrate use. The committee agreed that the potential impact of removing the PA for sildenafil should be assessed more completely before recommending any policy changes to Health Affairs. Bill Hudson (Humana) will present data from the MCSCs and MAJ Bellemin will present data from the NMOP at the next meeting for assessment of the potential impact of removing the sildenafil PA.

8. RATIONALE FOR QUANTITY LIMITS – COL Remund reported that the PEC will add to its website an explanation of the rationale for placing quantity limits on certain drugs.

9. PROPOSED QUANTITY LIMITS FOR OXYCONTIN – Bill Hudson (Humana) proposed a 120 tablet per 30 days quantity limit for oxycodone extended release (Oxycontin) for the NMOP and retail network due to increasing abuse and misuse of this product.

Some committee members stated that the quantity limit would adversely affect patients who have a legitimate need for large quantities of Oxycontin, and may have little or no impact on patients who are abusing or diverting it. Person who are abusing or diverting Oxycontin will more likely submit prescriptions to multiple pharmacies than a single prescription for a large quantity. Pharmacists can use the information in patient profiles and the advisory messages provided by PDTS to identify these patients. A quantity limit on Oxycontin may set a precedent for limits on other pain medications, which would be inconsistent with the movement toward more adequate treatment of pain. The committee voted against the proposed quantity limit.

10. REVIEW OF INJECTABLE MEDICATIONS AVAILABLE THROUGH THE NMOP – The PEC review of the NMOP Covered Injectables list identified goserelin (Zoladex) and leuprolide (Lupron) depot as items that are not labeled for self-administration or commonly used in an outpatient setting. During the 4-month period from Mar – Jun 2001, 15 patients received prescriptions for Zoladex and 63 patients received prescriptions for Lupron Depot from the NMOP.

Lupron is available in both subcutaneous and depot dosage forms and is indicated for a variety of disease states. The subcutaneous form is commonly administered in the home setting. Lupron Depot is an intramuscular injection and is not designed for self-administration, but several facilities have programs that teach caregivers to give IM dosage forms such as Lupron Depot at home (e.g., monthly injections for precocious puberty). The committee decided that both the subcutaneous and depot formulations of Lupron should remain on the NMOP Covered Injectables List.

Goserelin (Zoladex) is an implant that requires insertion under sterile conditions and is not routinely administered outside of a hospital or clinic. The assumption is that virtually all Zoladex prescriptions are taken to physician offices or clinics for administration. The committee's understanding is that TRICARE regulations and policies do not specifically prohibit patients from getting prescriptions filled at the NMOP or retail pharmacies for subsequent administration in a physician office or clinic. The committee decided that Zoladex should remain on the NMOP Covered Injectables List.

The committee then discussed numerous issues pertaining to patients obtaining injectable products from the NMOP or retail pharmacies for subsequent administration in provider offices or clinics:

- Safety concerns about patients transporting hazardous products such as cytotoxic agents
- Quality control concerns about products that are sensitive to heat or moisture
- Payment of unnecessary copays by patients if the injectable product should have been provided as part of the physician office visit
- Payment of excess costs by the government if the expense of the injectable product should have been covered as part of the payment for the office visit
- Coverage for drugs administered in provider offices under Medicare Part B for some patients
- The fact that some providers might not stock certain injectables in their offices, making it necessary for the patient to obtain these products from the NMOP or a retail pharmacy
- The need to allow for medical necessity overrides of any general policy concerning injectable medications. For example, some injectable drugs have clinically accepted uses via non-injectable routes of administration (e.g., colistin vials used for home nebulization).

COL Davies requested that the DoD P&T Committee provide a recommendation to TMA concerning any needed policy interpretations or policy changes. A subcommittee was appointed to work on this issue. Subcommittee members are: LtCol (select) George Jones (chair), LTC (P) Joel Schmidt, MAJ Brett Kelly, MAJ Mickey Bellemin, and Bill Hudson. LTC DeGroff will provide data from the Pharmacy Data Transaction Service to the workgroup. COL Remund noted that the data needs go beyond what PDTS could provide, since the workgroup also needed to know what drugs patients were having difficulty getting. MAJ Bellemin said that the NMOP had a list of complaints, while COL Davies can supply information from congressional complaints to TMA and some of the MCSCs have records of prescription denials.

11. CONTROLLED DISTRIBUTION OF DOFETILIDE (TIKOSYN) – Because of specialized educational requirements mandated by the FDA, dofetilide is only available for outpatient use through Stadtlander's Pharmacy/CVS Procare (which is a non-network pharmacy for DoD beneficiaries). LTC DeGroff reported that a centralized policy and procedure is being worked out with Pfizer so that DoD patients are not forced to pay the copay for a non-network pharmacy. Under the procedure, all prescriptions outside the MTF would still go through Stadtlander's/CVS Procare, but would be paid through a central billing mechanism. The patient would pay only the copay, with the rest billed to a central account at FSS pricing, and the drug would be mailed from Stadtlander's/CVS Procare to the patient. COL De Groff estimated that about 220 patients in DoD might use this process. Clinical reviews for dofetilide, which has multiple drug-drug interactions, are being done out of the PDTS database.

12. ADJOURNMENT – The meeting adjourned at 1200 hours. The next meeting will be held at 0800 on 15 November 2001 in the Washington DC area (specific location to be determined). All agenda items should be submitted to the co-chairs no later than 19 October 2001.

<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 or retail network formulary restrictions**	**BCF Status**
Almotriptan 6.25- and 12.5-mg tablets (Axert; Pharmacia & Upjohn)	7 May 01; treatment of migraine with and without aura in adults. Not intended for the prophylactic therapy of migraine or in the treatment of basilar or hemiplegic migraine. Safety and effectiveness in cluster headaches not established.	Added to NMOP Formulary	**Quantity Limits** **6.25-mg tab:** NMOP: 36 tablets per 90 days; Retail Network: 12 tablets per 30 days **12.5-mg tabs:** NMOP: 36 tablets per 90 days; Retail Network: 12 tablets per 30 days **Rationale for Quantity Limits** Safety and efficacy of treating more than 4 migraines a month with this class of drugs not established. Patients experiencing more frequent migraines are likely to be candidates for routine prophylactic treatment (e.g., with beta-blockers or selective serotonin reuptake inhibitors). Recommended quantity limits for the retail network are based on the treatment of 4 headaches a month, rounding up to the next full box, if necessary. Quantity limits for the NMOP were calculated as three times the limit for the retail network to maintain consistency across points of service. **Prior Authorization** No	Not added to the BCF **BCF drugs in this class:** sumatriptan oral and sumatriptan autoinjector
Drospirenone 0.3 mg / ethinyl estradiol 30 mcg tablets (Yasmin; Berlex)	11 May 01; prevention of pregnancy	Added to NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **BCF drugs in this class**: multiple oral contraceptives
Desogestrel/ ethinyl estradiol tablets (Cyclessa; Organon)	22 Dec 2000; prevention of pregnancy	Added to NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **BCF drugs in this class:** multiple oral contraceptives
Valganciclovir tablets (Valcyte; Syntex)	29 March 2001; treatment of cytomegalovirus retinitis in AIDS patients	Added to NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **BCF drugs in this class:** None

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**NMOP Formulary Status**	**NMOP or retail network formulary restrictions**	**BCF Status**
Albuterol sulfate 3 mg and ipratropium bromide 0.5 mg per 3 mL (DuoNeb Solution for Inhalation; Dey Labs)	21 Mar 2001; bronchospasm associated with COPD in patients requiring more than one bronchodilator medication	Added to NMOP Formulary	**Quantity Limits** NMOP: 540 vials per 90 days; retail network: 180 vials per 30 days **Rationale for Quantity Limits** Based on maximum recommended doses (up to 6 treatments per day). Quantity limits for both ipratropium and albuterol vials for inhalation are currently in effect. **Prior Authorization** No	Not added to the BCF **BCF drugs in this class:** albuterol and ipratropium vials for inhalation
Insulin aspart injection (NovoLog; Novo Nordisk)	8 Jun 2000 (available Sep 2001); with an intermediate or long-acting insulin for treatment of adult patients with diabetes mellitus or those with hyperglycemia	Added to the NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **BCF drugs in this class:** No rapid-acting insulin analogs on the BCF; insulins on the BCF are Novolin N, R, 70/30

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** (See Minutes of the 15 August DoD P&T Executive Council Meeting)
   A. *Additions to the BCF*
      1) Rabeprazole oral – effective 1 Oct 2001
      2) Montelukast oral
      3) Amiodarone oral
      4) Clindamycin phosphate 1% topical solution
   B. *Deletions from the BCF*
      1) Cerivastatin oral – due to market withdrawal
      2) Omeprazole oral – effective 1 Oct 2001
      3) Quinidine sulfate oral
      4) Quinidine gluconate oral
      5) Primidone oral
   C. *Changes and clarifications to the BCF*
      1) The PPI class will be open effective 1 Oct 2001. As of 1 Oct 2001, MTFs must add rabeprazole (Aciphex) to their formularies (see above), but may have other PPIs on their formularies in addition to rabeprazole.
2. **NMOP FORMULARY CHANGES**
   A. *Additions to the NMOP Formulary* (See Appendix A for details)
      1) Almotriptan tablets (Axert; Pharmacia & Upjohn) - quantity limits apply
      2) Drospirenone 0.3 mg and ethinyl estradiol 30 mcg tablets (Yasmin; Berlex)
      3) Desogestrel 0.1/0.125/0.15 mg and ethinyl estradiol 25 mcg tablets (Cyclessa; Organon)
      4) Valganciclovir tablets (Valcyte; Syntex)
      5) Albuterol sulfate 3 mg and ipratropium bromide 0.5 mg per 3 mL (DuoNeb Solution for Inhalation; Dey Labs) – quantity limits apply
      6) Insulin aspart injection (NovoLog; Novo Nordisk)
   B. *Exclusions from the NMOP Formulary* – None
3. **QUANTITY LIMIT CHANGES (NMOP AND RETAIL NETWORK)**
   A. Quantity limit for almotriptan 6.25- and 12.5-mg tablets (Axert; Pharmacia & Upjohn) – NMOP: 36 tablets per 90 days; retail network: 12 tablets per 30 days
   B. Quantity limit for albuterol sulfate 3 mg and ipratropium bromide 0.5 mg per 3 mL (DuoNeb Solution for Inhalation; Dey Labs) – NMOP: 540 vials per 90 days; retail network: 180 vials per 30 days
4. **CHANGES TO THE PRIOR AUTHORIZATION PROGRAM (NMOP AND RETAIL NETWORK)** – None

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MCCS-GPE **15 August 2001**

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 15 August 2001 at the Non-Commissioned Officers Club, Ft. Sam Houston, TX. The DoD P&T Executive Council is responsible for performing certain inherently governmental functions relevant to the DoD pharmacy benefits program. The Council focuses primarily on issues related to the Basic Core Formulary (BCF), national pharmaceutical contracts, and blanket purchase agreements. The DoD P&T Executive Council is comprised of federal employees who are members of the DoD P&T Committee.

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
LtCol (select) 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, MS	Army
CAPT Robert Rist	Coast Guard
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
LTC Mike Kieffer, MS	Joint Readiness Clinical Advisory Board representative

MEMBERS ABSENT

COL Rosa Stith, MC	Army
Dick Rooney	Department of Veterans Affairs

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TRICARE Management Activity
COL Mike Heath, MS	Army Pharmacy Consultant; Chair, DoD Pharmacy Board of Directors
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
LtCol Gary Blamire, MSC	Lead Agent Office, Region 6
LTC Don De Groff, MS	DoD Pharmacoeconomic Center
LTC Doreen Lounsbery, MC	DoD Pharmacoeconomic Center
LtCol Ed Zastawny, BSC	DoD Pharmacoeconomic Center
LCDR Ted Briski, MSC	DoD Pharmacoeconomic Center
MAJ Cheryl Filby, MS	Defense Supply Center Philadelphia
MAJ Barbara Roach, MC	DoD Pharmacoeconomic Center
SFC Tom Bolinger	DoD Pharmacoeconomic Center
SFC Augustin Serrano	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
Dave Bretzke	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
Carol Scott	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
Paul Vasquez	Defense Supply Center Philadelphia

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

4. ADVANCES IN MEDICAL PRACTICE (AMP) PROGRAM

TMA recently released AMP funds for FY 2001 to the military services. Based on prime vendor data, MTFs spent $37.3 million on AMP drugs during the first nine months of FY 2001 (see Appendix A). Total AMP expenditures for FY 2001 will likely be close to the projected figure of $50 million.

5. PROGRAM BUDGET DECISION 812

Program Budget Decision (PBD) 812, approved by the Deputy Secretary of Defense on 21 June 2001, increases MTF pharmacy funding by $307.1 million in FY 2002 to recognize the cost growth experienced in FY 2001. PBD 812 also funds MTF pharmacies at a 15% annual growth rate through FY 2007. MTF pharmacy expenditures will be reviewed annually to determine the adequacy of the revised program funding, and it will be adjusted accordingly. The PBD recognizes the fact that inadequate funding of MTF pharmacies can cause beneficiaries to fill their prescriptions in the private sector at much higher cost to the government.

6. COX-2 INHIBITORS

At the last meeting, the Council agreed that management of the COX-2 inhibitors should ideally focus on two issues: accurately and efficiently targeting COX-2 therapy to those patients at greatest risk for gastrointestinal (GI) adverse events, and reducing the unit cost of COX-2 inhibitors.

A. *Formulary status of COX-2 inhibitors and the use of targeting programs at MTFs*

A PEC survey of MTFs in August 2001 found that 54% of the MTFs have no COX-2 inhibitors on formulary and 77% of the MTFs have a program to target COX-2 inhibitor therapy (see Table 1). Most MTFs use the NMOP prior authorization criteria to target therapy.

Table 1: Formulary Status and Targeting Programs for COX-2 Inhibitors at MTFs

Service	MTFs responding	COX-2s on formulary			MTFs with Targeting Program
		None	One*	Both	
Navy	**14**	12	0	2	8
Air Force	**19**	6	7	6	19
Army	**25**	13	4	8	18
Total	**58**	**31 (53%)**	**11 (19%)**	**16 (28%)**	**45 (78%)**

* 10 MTFs had celecoxib and 1 MTF had rofecoxib

B. *Use of COX-2 inhibitors in the Military Health System (MHS)*

Table 2 displays the number of prescriptions filled for COX-2 inhibitors and traditional NSAIDs at the various MHS outpatient pharmacy points of service during July 2001.

Table 2: Prescription fills for COX-2 Inhibitors and Traditional NSAIDs in the MHS, July 2001

	MTF prescriptions	MCSC retail network prescriptions	NMOP prescriptions	Total
COX-2 inhibitors	45,345 (13%)	40,094 (37%)	12,826 (43%)	98,265 (20%)
Traditional NSAIDs	298,799 (87%)	67,960 (63%)	17,306 (57%)	384,065 (80%)
Total	344,144	108,054	30,132	482,330

Source: Pharmacy Data Transaction Service Customer Service Support Center

C. *Therapeutic interchangeability of COX-2 inhibitors*

A significant reduction in unit cost would likely be achieved by a closed class contract that selects a single COX-2 inhibitor for the BCF, but a closed class contract is feasible only if the drugs are therapeutically interchangeable. Additional safety data concerning rofecoxib and celecoxib recently became available due to the release of FDA advisory committee briefing documents and reviews of additional data from two large trials—the Vioxx Gastrointestinal Outcomes Research (VIGOR) study and the Celecoxib Long-term Arthritis Safety Study (CLASS). These data were submitted to the FDA Arthritis Advisory Committee to support manufacturers' requests to remove NSAID-class GI warnings from product labeling. (The review documents represent the opinions of reviewers and not final conclusions of the FDA, which has not yet made a final determination.) The Council assessed various concerns about the therapeutic interchangeability of celecoxib and rofecoxib, including two key issues that arose from review of this additional information.

1. *Vioxx Gastrointestinal Outcomes Research study (VIGOR)* – Data from the VIGOR trial showed an increased risk of serious thrombotic cardiovascular events for rofecoxib compared to naproxen. The rate of confirmed thrombotic cardiovascular serious adverse events was 1.67 per 100 patient-years for the rofecoxib group and 0.70 per 100 patient-years for the naproxen group (RR 2.37; 95% CI 1.39 – 4.06; p=0.0016). The difference in the composite measure was primarily due to a difference in the incidence of myocardial infarctions between the rofecoxib and the naproxen group. These results could be explained by either a prothrombotic effect of rofecoxib or an antithrombotic cardioprotective effect of naproxen. See Appendix B for a more detailed discussion of VIGOR results.
2. *Celecoxib Long-term Arthritis Safety Study (CLASS)* – Published results of the CLASS trial were limited to data obtained during the first six months of study participation, although about 35% of patients completed nine months or more of treatment. Published results did not show a significant difference in the primary endpoint of the study [annualized incidence of confirmed complicated UGI events (perforations, obstructions, and GI bleeds)] between celecoxib and the pooled group of comparator non-steroidal anti-inflammatory drugs (NSAIDs) in the overall study population. There was a significant difference in the primary endpoint in the subgroup of patients not taking low dose aspirin.

   Results from the entire study period did not show a significant difference for the primary endpoint in either the overall study population or in the subgroup of patients not taking aspirin. The differences between the six-month and entire study period data appeared to be due to the occurrence of relatively more confirmed complicated UGI events in the celecoxib group than in the NSAID group in the time period subsequent to the first six months of study participation.

   These results raise doubts about the GI protective effects of celecoxib. The additional data also suggest that the statistically significant differences in GI safety endpoints between celecoxib and the pooled NSAID group are primarily due to differences between celecoxib and ibuprofen; celecoxib was not statistically significant from diclofenac for any patient group or endpoint. This finding raises additional doubts about the generalizability of CLASS results to patients receiving "traditional" NSAIDs not tested in the CLASS trial. See Appendix B for a more detailed discussion of CLASS results.
3. *Lack of rheumatoid arthritis indication for rofecoxib* – Rofecoxib is not currently indicated for rheumatoid arthritis (RA). Merck filed an application for a supplemental NDA for an indication for RA in March 2001 and has submitted additional studies to the FDA.
4. *Edema and hypertension* – Like traditional NSAIDs, both celecoxib and rofecoxib have been shown to increase blood pressure and produce edema. It is not clear whether there is a clinically significant difference in the propensity of the two drugs to produce such effects. Studies suggest a small, dose-related increase in edema and hypertension with rofecoxib, especially at 50 mg QD. A dose-response relationship has not been clearly shown for celecoxib.

5. *MTF survey regarding therapeutic interchangeability* - A survey was sent to lead agent pharmacists to ascertain the opinions of MTFs in their regions. The survey focused on the consensus opinions of facility P&T committees, not individual provider opinions. Lead agent pharmacists had the option of reporting individual MTF responses or submitting a single consensus response from their entire region. The survey included a clinical review comparing celecoxib and rofecoxib and a fact sheet outlining possible scenarios for contracting and/or BCF status. Questions about possible contracting and/or BCF status were to be answered under the assumption that the Program Budget Decision 812 would provide MTFs with adequate funding for these agents. Responses to the survey are summarized in Table 3.

Table 3: Responses to the COX-2 Interchangeability Survey

Region			1	2	3	4	5	6	7/8	9	10	11	12	Summary
Number of facilities responding			12	5	4	0	*	6	*	2	4	2	11	
% of patients whose initial clinical needs are met by	Celebrex	>90%	5	2	2			4		0	1	1	5	20
		75-90%	3	1	0			1		0	3	0	4	12
		<75%	3	2	2		X	1	X	2	0	1	2	14
	Vioxx	>90%	6	2	2			3		0	2	1	6	18
		75-90%	1	2	0			1	X	1	2	0	3	10
		<75%	4	1	2		X	2		1	0	1	2	12
Product more likely to fail		Equal	10	4	4		X	1		1	2	1	10	34
		Celebrex	1					1	X		1		1	5
		Vioxx								1	1			2
Relative acceptability of management options – means of individual responses (1 = Most acceptable; 5 = Least acceptable)														
Closed class contract			3.5	4	2.5		2	1	3		5	3	1.5	2.8
Add specific agent in open class			2	2	2.5		3	3	2	1.5	2	2	1.5	2.2
Add requirement for agent but do not specify			1	1	4		5	2	1	1.5	1	4	3.5	2.4
Add both agents to BCF			3.5	3	5		4	5	4		3	5	5	4.1
Add neither agent to BCF			5	5	1		1	4	5		4	1	3.5	3.3

* Consensus response from entire region only

D. *VA/DoD Clinical Review*

The PEC and the VA PBM are collaborating on a clinical review of the COX-2 inhibitors, but the review is not complete yet.

E. *P&T Executive Council Conclusions*

Based on the available safety and efficacy data and the lack of a RA indication for rofecoxib, the Council could not conclude that celecoxib and rofecoxib are therapeutically interchangeable. MTFs vary significantly in their support for a closed class contract. The Council does not support a closed class contract for a COX-2 inhibitor at this time.

The analysis of all the data for the CLASS study raises questions about the GI protective effects of celecoxib. The VIGOR study raises concerns about a potential increase in risk of cardiovascular events with rofecoxib. The COX-2 inhibitors are no more effective than traditional NSAIDs for treating osteoarthritis or rheumatoid arthritis. The COX-2 inhibitors cost much more than traditional NSAIDs. The Council concluded that a COX-2 inhibitor should not be added to the BCF at this time.

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

A. *Contract awards, renewals, and terminations*

- As of 1 August 2001, 47 joint VA/DoD national contracts have been awarded. Information on national pharmaceutical contracts, including NDC numbers and prices, is available on the DSCP website (www.dmmonline.com).
- Since the last meeting, DoD/VA single source contracts were awarded for the following drugs:
  - Carbidopa/levodopa 25 mg/100 mg and 50 mg/200 mg sustained action tablets, to Dupont Pharma
  - Glyburide 1.25mg, 2.5mg and 5mg tablets, to Pharmacia Corporation
  - Ointment Base (Absorbase 50% water-in-oil emulsion) 454- and 120-gram jars, to Carolina Medical Products
- The 21-count, 6-cycle package of ethinyl estradiol/ norethindrone tabs (Norinyl) was removed from the national contract effective 24 July 2001. The item may be purchased off the FSS at the same price. The 28-count packages remain on the contract.
- The albuterol inhaler contract will not be renewed due to continuing availability problems with all the chlorofluorocarbon (CFC) albuterol products.

B. *Financial impact of contracts* – Cost avoidance has been estimated by subtracting the actual expenditures for the "market basket" of products affected by a contract from the expenditures that would have occurred if the contract did not exist (based on the prices that existed before the contract took effect). This method is reasonably accurate for the first year of a contract, but changes in the "market basket" of products (e.g., new indications, generic availability, price changes for non-contracted drugs, introduction of new products, product withdrawals, etc.) make it difficult to accurately estimate "what would have been paid" if the contract did not exist in subsequent years. The Council agreed that the cost per patient-day of therapy or cost per member per month within therapeutic categories would be useful indicators of the financial impact of national pharmaceutical contracts and would avoid the ambiguities of cost avoidance estimates.

C. *Statin Contract* - The withdrawal of cerivastatin (Baycol) from the market leaves simvastatin (Zocor) as the only statin on the Basic Core Formulary (BCF) and the National Mail Order Pharmacy (NMOP) formulary. The P&T Executive Council concluded that simvastatin could meet the clinical needs of the vast majority of patients who previously took cerivastatin, so there is no need to add a second statin to the BCF or NMOP formulary at this time. Patients who previously took cerivastatin should be switched to simvastatin. Other statins should be used only when simvastatin will not meet the clinical needs of an individual patient.

The simvastatin contract requires the statin class to remain "closed" on the BCF and NMOP formulary. The simvastatin contract is in effect until February 2002, and there is an option to renew the contract to February 2003. The DoD P&T Executive Council will evaluate clinical and economic information regarding the statin class and make a

recommendation to the Defense Supply Center Philadelphia (DSCP) regarding the potential renewal of the simvastatin contract. The Council will consider the impact of new NCEP guidelines on statin usage; the potential availability of rosuvastatin (Crestor); and impending patent expirations (lovastatin - expected Dec 2001; pravastatin - expected early 2003).

The P&T Executive Council was informed that Merck would reduce the DoD contract prices for four of the five strengths of simvastatin effective 1 Sep 2001 (see Table 4).

Table 4: DoD Contract Prices for Simvastatin

Strength	Old Price	New Price (effective 1 Sep 01)
5 mg	$0.41	$0.38
10 mg	$0.62	$0.50
20 mg	$0.65	$0.60
40 mg	$0.94	$0.85
80 mg	$0.98	$0.98

D. *Proton pump inhibitor contract*

The contract for omeprazole (Prilosec) will expire on 30 September 2001 and will not be renewed because the omeprazole contract price would be much higher than the prices for other proton pump inhibitors. As a consequence, the proton pump inhibitor class will revert to an "open class" on the BCF as of 1 October 2001. The Council reviewed the safety, tolerability, efficacy, price/cost, and other factors associated with proton pump inhibitors.

Safety/Tolerability – The PPIs appear to have similar safety profiles. Early concerns about gastric enterochromaffin-cell hyperplasia and gastric cancer caused by chronic hypergastrinemia have not materialized in clinical practice.

Omeprazole may be the most likely to cause cytochrome P450 drug interactions as it interacts preferentially with CYP2C19, inhibiting the metabolism of diazepam, phenytoin, and warfarin. Rabeprazole, pantoprazole and lansoprazole do not appear to cause clinically significant P450 drug interactions. Experience with esomeprazole is limited. Omeprazole is Pregnancy Category C; the other 4 PPIs are Category B.

Efficacy – When used at appropriate doses, all the PPIs are efficacious for the treatment of a variety of acid-related disorders, including gastroesophageal reflux disease (GERD) and erosive esophagitis. More than 20 published, double-blind, randomized, head-to-head trials used omeprazole as the comparator drug. These studies showed that, in most patients, omeprazole 20 mg/day, lansoprazole 30 mg/day, pantoprazole 40 mg/day, esomeprazole 40 mg/day, and rabeprazole 20 mg/day relieve GERD symptoms within several days and heal esophageal erosions within 4 - 8 weeks of initiating therapy. Reported differences in the duration of antisecretory effect vary between patients and do not necessarily translate into improved clinical efficacy. Lansoprazole 30 mg/day and rabeprazole 20 mg/day may provide more rapid relief of GERD symptoms when compared with omeprazole 20

mg./day, but the differences are usually observed only in the first few days of treatment. Esomeprazole may have a faster onset of healing of esophageal erosions, but healing rates at 12 weeks are similar to those reported with omeprazole.

Price/Cost

Table 5: DoD Prices for Proton Pump Inhibitors

Generic	Brand	Dose	Current Price	After 1 Oct
Rabeprazole	Aciphex	20 mg	$0.22 (FSS)	$0.22 (FSS)
Lansoprazole	Prevacid	30 mg	$2.06 (FSS)	$2.06 (FSS)
Pantoprazole	Protonix	40 mg	$1.27 (FSS)	$1.27 (FSS)
Omeprazole	Prilosec	20 mg	$1.09 (contract)	$2.02 (FSS)
Esomeprazole	Nexium	20 mg	$2.35 (FSS)	$2.35 (FSS)
FSS = Federal Supply Schedule; BPA = Blanket Purchase Agreement				

Other Factors

- *Availability of generic omeprazole* – AstraZeneca has received pediatric exclusivity for Prilosec through 5 Oct 2001. The FDA has granted tentative approval for generic versions of Prilosec to two generic companies: Andrx for 10-, 20- and 40-mg delayed release capsules and GenPharm for 10- and 20-mg delayed release capsules. Due to an agreement between the two companies, Andrx would be considered the "first-to-file" and thus should be the only generic available for the most commonly used 20-mg strength of omeprazole for up to 180 days following approval. It is unknown when generic omeprazole will be available, as lawsuits involving at least 4 generic companies are underway or pending.
- *VA usage* - The VA is currently converting the majority of their patients from lansoprazole, which was previously their contract agent, to rabeprazole. Lansoprazole continues to be available to VA facilities at a BPA price of $0.55 per capsule.
- *Direct-to-consumer (DTC) advertising* - AstraZeneca is currently running an intensive DTC advertising campaign attempting to convince patients to switch from omeprazole to esomeprazole.
- *Provider survey results* – A survey was sent to GI specialists and primary care providers in all three services, who were also asked to forward the survey to other clinicians. The VA PPI class review and a supplemental fact sheet from the PEC were sent along with survey questions. A total of 28 responses were received from 15 Army, 11 Air Force, and 2 Navy providers. The majority of responses were from family medicine (10), followed by GI specialists (6); general surgery (3); internal medicine, primary care, flight medicine, unknown specialty (2 each); and pulmonary/critical care (1). Summary results are shown in Table 6 following.

  Comments from providers generally supported the therapeutic interchangeability of PPIs. Most agreed that using the least costly PPI would be appropriate to treat the majority of patients.

Several providers mentioned the need for alternate PPIs for patients with swallowing difficulties. Only lansoprazole has an oral suspension. Labeling for lansoprazole, omeprazole, and esomeprazole capsules indicates they can be opened and sprinkled on applesauce; rabeprazole and pantoprazole have no alternative dosage forms, but are relatively small tablets. Providers also mentioned the desire to have an intravenous PPI available. Only pantoprazole is available in an intravenous formulation.

Two providers commented negatively on the DTC campaign for esomeprazole. Two Air Force providers mentioned the fact that omeprazole is the only PPI specifically approved for Air Force aircrew waiver.

Table 6: PPI Provider Survey

	Strongly Agree	Agree	Neither Agree or Disagree	Disagree	Strongly Disagree
All the PPIs currently available are likely to be effective for treating the conditions for which I typically prescribe PPIs.	14	13	0	1	0
The differences in FDA-approved indications between these products have little clinical relevance when treating most patients.	8	17	0	3	0
The faster time to relief of symptoms reported by AstraZeneca for esomeprazole has little to no clinical significance.	5	16	4	2	0
The faster time to relief of symptoms reported for rabeprazole has little to no clinical significance.	4	16	5	2	0
Price should be a consideration when providers decide which of these agents to prescribe.	13	14	1	0	0
I have sufficient concerns regarding the safety, efficacy, or patient acceptability of the other available PPIs that I will continue to prescribe Prilosec after October 1st regardless of price.	0	2	0	13	12

After considering safety, tolerability, efficacy, price, and patient acceptability, which of the following PPIs, if available on formulary after October 1, would I feel comfortable using.

Drug	Definitely Use	Consider Use	Use with reservations	Never Use
Omeprazole	14	7	3	1
Rabeprazole	18	8	1	0
Lansoprazole	13	13	0	0
Pantoprazole	7	16	2	1
Esomeprazole	8	8	5	3

The Council concluded that there are no clinical or economic reasons to pursue another closed class contract in this drug class. The Council voted to remove Prilosec from the BCF and add rabeprazole (Aciphex) to the BCF. These BCF changes take effect on 1 Oct 2001. MTFs may have other PPIs on their formularies in addition to rabeprazole as of 1 Oct 2001.

E. *Status of contracting initiative for nasal corticosteroid inhalers* – The DoD P&T Executive Council concluded at the November 2000 meeting that a closed class contract could be sought for a high-potency aqueous nasal corticosteroid. The Council identified five products that could compete for the contract: budesonide 32 mcg/spray, fluticasone 50 mcg/spray, triamcinolone 55 mcg/spray, mometasone 50 mcg/spray, and beclomethasone 84 mcg/spray. The VA recently completed its class review of nasal corticosteroid inhalers. The VA wants to include flunisolide (Nasarel) in the solicitation for a closed class contract. The Council asked the PEC to update its analysis of the nasal steroid class and recommend to the Council whether or not flunisolide should be included in the solicitation.

F. *Status of potential contracting initiative for leukotriene antagonists* – The VA is currently evaluating montelukast (Singulair) and zafirlukast (Accolate) for potential contracting. The 5-lipoxygenase inhibitor Zileuton (Zyflo) is not being considered due to several clinical disadvantages, including four times daily dosing and an increased risk of drug interactions and hepatotoxicity compared to the other two agents. This drug class has been proposed as a potential joint DoD/VA contracting initiative. The BCF currently states that each MTF must have a leukotriene antagonist on formulary, but the selection of the specific product is left to the MTF.

Safety/Tolerability – Placebo-controlled trials with both agents have shown a low incidence of adverse effects. GI symptoms and headache are reported most commonly. In trials comparing leukotriene antagonists with inhaled corticosteroids, both montelukast and zafirlukast were associated with higher discontinuation rates due to adverse events than inhaled corticosteroids.

Both products have been associated with elevations in liver function tests, although confounding factors make causality difficult to assess. One serious adverse reaction, Churg Strauss syndrome, has occurred during steroid tapers with both montelukast and zafirlukast, but may have been associated with "unmasking" of a pre-existing condition. Zafirlukast has clinically significant drug interactions with theophylline and warfarin. Clinically significant drug interactions have not been reported for montelukast.

Efficacy

Adult patients

- *Comparative trials with inhaled ß-agonists*: Studies have shown that adding a leukotriene antagonist to a short acting ß-agonist reduces the occurrence of asthma symptoms and the use of ß-agonists more than placebo.
- *Comparative trials vs. inhaled corticosteroids*: Although similar asthma exacerbation rates have been reported, inhaled corticosteroids significantly improve quality of life, lung function, and symptom control compared with the leukotriene antagonists.
- *Asthma monotherapy trials*: There are no published head-to-head trials with zafirlukast and montelukast. When two individual studies with similar trial design are compared, montelukast was slightly superior to zafirlukast in terms of FEV1 (forced expiratory volume in one second), PEFR (peak expiratory flow rate), and

prn albuterol use at 12 weeks. However, low-dose fluticasone was superior to either leukotriene inhibitor.

- *Combination of leukotriene antagonists with inhaled corticosteroids*: There are no head to head comparisons, and the trial designs of the available studies are too dissimilar to make comparisons

Pediatric patients

- Head to head comparisons between montelukast and zafirlukast are not available. The trial that was the basis for montelukast's pediatric labeling is only available in the package insert and has not been published in a peer-reviewed journal. A pediatric study comparing zafirlukast with low-dose fluticasone has been published. Both montelukast and zafirlukast improve symptoms and lung function compared with placebo. Inhaled steroids show similar exacerbation rates compared to leukotriene antagonists, but result in better improvements in lung function and symptoms.

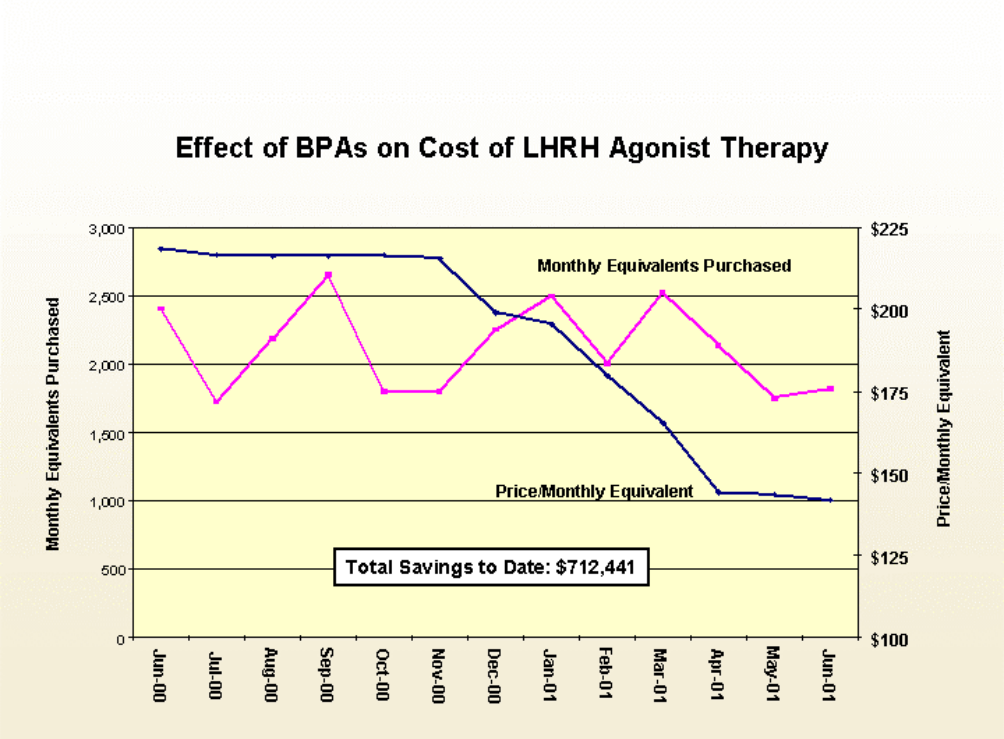
Other Factors

- Based on total tablets purchased, market shares for montelukast and zafirlukast in DoD MTFs are approximately 93% and 7%, respectively. Purchases by VA facilities are more evenly split between the two drugs—43% of leukotriene antagonist tablets purchased are montelukast; 56% are zafirlukast. Zafirlukast is typically dosed twice daily.
- Montelukast is dosed once daily and has FDA approval for patients as young as 2 years of age. A 4-mg chewable tablet formulation is available for children 2-5 years of age. Zafirlukast is dosed twice daily. It is FDA-approved for patients 7 years of age and older.

The Council concluded that montelukast and zafirlukast are not therapeutically interchangeable and that a closed class contract for a leukotriene inhibitor is not feasible for DoD. After considering the safety, tolerability, efficacy, and other factors associated with the leukotriene antagonists, the Council voted to add montelukast to the BCF.

G. *Non-sedating antihistamine contract* – Increases in prescription market share for fexofenadine (Allegra) and decreases in market share for loratadine (Claritin) indicate that MTFs are successfully implementing the non-sedating antihistamine contract. By the end of July 2001, the market share for fexofenadine (as a percent of all prescriptions for non-sedating antihistamines dispensed at MTF pharmacies) increased from 50% prior to the contract to nearly 80%. The prescription market shares for fexofenadine and loratadine remained stable in the retail pharmacy networks and the NMOP, indicating that MTFs are maximizing the use of fexofenadine without shifting loratadine prescriptions into the retail pharmacy network or NMOP. Since the contract took effect, the average cost per non-sedating antihistamine tablet/capsule purchased by MTFs has dropped by 33%, from $0.87 to $0.58. Appendix C contains market share and cost graphs for the non-sedating antihistamines.

H. *Status of BPAs and potential contracting action for Leutinizing Hormone Releasing Hormone (LHRH) agonists* – The AstraZeneca Federal Account Director has stated that the Blanket Purchase Agreement (BPA) for goserelin (Zoladex) will stay in effect even if the 80% market share requirement is not met by 1 Sep 2001. The Zoladex and leuprolide (Lupron) BPAs have reduced the weighted average cost per monthly equivalent of LHRH agonist therapy for prostate cancer by 35%, from $215 in November 2000 to $140 in June 2001. The BPAs yielded $712,000 in cost avoidance for MTFs from November 2000 to June 2001.



Lupron and Zoladex are generally considered equivalent in safety and efficacy for treatment of prostate cancer. The therapeutic interchangeability of these products hinges on tolerability and other factors that affect patient or provider acceptance of either product. CAPT Torkildson (PEC) obtained input from Urology specialty leaders and other providers:

- Several providers reported that patients had been switched from one product to the other without problems.
- Zoladex must be implanted rather than simply injected, so administration of Zoladex consumes more physician time. Some MTFs improve the efficiency of Zoladex administration by training non-physicians to administer the product.
- Lupron has a 4-month dosage form; Zoladex does not.
- Some providers expressed concern regarding lack of experience with one or the other products.
- There was general agreement that the potential for decreased cost is sufficient reason to seek a contract.

The dosage forms of Lupron and Zoladex that would compete for this contract are not used exclusively for prostate cancer. The PEC estimates that 10% of the Lupron usage and 2% of the Zoladex usage are for conditions other than prostate cancer. However, the age and sex specificity of prostate cancer allows contract compliance to be monitored relatively easily.

The Council voted to support a joint VA/DoD contract for an LHRH agonist for the treatment of prostate cancer.

8. THE CLOPIDOGREL IN UNSTABLE ANGINA TO PREVENT RECURRENT EVENTS (CURE) TRIAL

The Council reviewed preliminary summary information from the CURE trial. (Complete results of the trial were subsequently published in the 16 Aug 2001 issue of the New England Journal of Medicine.) The CURE trial enrolled approximately 12,500 patients with unstable angina and non-ST elevation MI presenting within 24 hours of the onset of symptoms. Patients were randomized into two groups: aspirin alone (75 to 325 mg QD) or aspirin plus clopidogrel (300 mg immediately, then 75 mg QD). Follow-up was for an average of 9 months. A 20% reduction in the composite endpoint of cardiovascular death, nonfatal MI, or stroke was reported for the combination of clopidogrel plus aspirin compared to aspirin alone. The combination reportedly had both an early (within 2 hours) and sustained benefit relative to aspirin alone. A significant increase in major (but not life-threatening) bleeds was reported in patients receiving both aspirin and clopidogrel, but there was insufficient information to adequately assess the severity of the incremental risk of bleeding.

Clopidogrel is currently indicated for prevention of stroke and/or MI in patients with aspirin allergy and for short-term use following cardiac stent placement. Clopidogrel is not on the BCF. The Council agreed that it would be premature to consider clopidogrel for the BCF on the basis of preliminary data, but asked the PEC to review results of the published study and make recommendations.

9. MTF REQUESTS FOR BCF CHANGES

A. *Request to remove quinidine from the BCF* – A pharmacist from an Army medical center requested removal of quinidine products from the BCF due to infrequent usage.

Meta-analyses have shown increased mortality rates in patients given quinidine during or after acute myocardial infarction and patients given quinidine after cardioversion for atrial fibrillation. Mortality rates in patients with ventricular arrhythmias were three times higher with quinidine than other Class I antiarrhythmics. In addition, the risk of torsade de pointes, a potentially fatal arrhythmia, is estimated to be 1.5% to 8% in patients treated with quinidine. (Some clinicians feel this may underestimate the true occurrence.) Current therapy recommendations relegate quinidine to second or third-line status for either atrial or ventricular arrhythmia. According to data from the Uniformed Services Prescription Database, MTF prescriptions for quinidine products have consistently decreased over the past 3 years to fewer than 200 prescriptions per month for quinidine sulfate and fewer than 1300 prescriptions per month for quinidine gluconate.

The Council voted to remove both quinidine sulfate and quinidine gluconate from the BCF. MTFs may choose to remove or retain these products on their formularies.

B. *Request to remove primidone from the BCF* – A pharmacist from an Army medical center requested removal of primidone from the BCF due to infrequent usage.

Primidone is FDA approved for treatment of partial complex seizures but is rarely used for that indication. Its primary use is off-label for the treatment of essential tremor. Safer, more tolerable alternatives are available for both seizure disorder and essential tremor. The DoD P&T Council voted to remove primidone from the BCF because it has no clinical benefit over agents already on the formulary. MTFs may choose to remove or retain primidone on their formularies.

C. *Request to add amiodarone to the BCF* – A primary care provider and a cardiologist from an Air Force teaching facility requested addition of amiodarone to the BCF based on current use of this drug in clinical practice.

Safety/Tolerability - Amiodarone carries a black box warning that lists potentially fatal toxicities, including proarrhythmic effects, pulmonary toxicity (hypersensitivity pneumonitis or interstitial/alveolar pneumonitis), and overt liver disease (in a few cases). Proarrhythmic effects appear to occur in less than 1% of patients, mostly in conjunction with electrolyte abnormalities or when used concurrently with other antiarrhythmics. This is a less frequent occurrence than seen in other antiarrhythmics. Pulmonary toxicity can be seen in 5% to 15% of patients, but has a good prognosis when the drug is discontinued.

The most common adverse effect of amiodarone is thyroid dysfunction; discontinuation of the drug is usually not necessary. Most other adverse effects are dose dependent. In general, smaller doses of amiodarone are required to treat atrial arrhythmias than ventricular arrhythmias. No other Class III antiarrhythmics are currently available.

Efficacy – Amiodarone is only FDA-indicated for the management of life-threatening recurrent ventricular fibrillation or hemodynamically unstable ventricular tachycardia, but use of the drug in clinical practice has changed significantly since its introduction in 1985. Amiodarone is now widely used to treat both atrial and ventricular arrhythmias. .

Other Factors – The VA developed a form to assist in monitoring amiodarone patients with regard to drug-drug interactions and timing of labs and other ancillary services (available at: www.vapbm.org/monitoring/amiodaron.htm). Guidelines intended for the use of primary care providers who follow patients on amiodarone have been issued by the North American Society of Pacing and Electrophysiology [Arch Intern Med 2000 (26 June); 160(12):1741-8]. Publication of guidelines for the treatment of atrial fibrillation by the American College of Cardiology and the American Heart Association are anticipated by the end of Aug 2001.

The Council added amiodarone to the BCF.

10. REVIEW OF ACNE MEDICATIONS FOR THE BCF

MAJ Barbara Roach reported on the PEC review of acne medications. The BCF currently lacks topical treatment choices for patients with acne who do not respond to over-the-counter benzoyl peroxide. The PEC evaluated the safety, tolerability, efficacy, cost, and historical MTF usage of topical acne medications and recommended the addition of clindamycin phosphate 1% solution and tretinoin cream 0.025% and 0.05% to the BCF. The PEC also recommended the removal of age restrictions for tretinoin cream in the NMOP and retail

pharmacies because it is commonly used for seborrheic keratoses (which occur in older adults).

The Council added clindamycin phosphate 1% solution to the BCF. Council members were concerned that the removal of age restrictions would allow tretinoin to be used for cosmetic treatment of photoaged skin (wrinkles and liver spots). The Council was uncertain as to whether the age restriction was specified in the Code of Federal Regulations, TRICARE policy, or the NMOP Statement of Work. Military service policies might also have age limits on tretinoin availability. The Council voted to table the decision on tretinoin until these issues are clarified.

11. OBTAINING INPUT FROM PROVIDERS

The PEC has substantially increased efforts to obtain input from physicians and pharmacists on formulary and contracting issues. A BCF request form is available for MTF personnel to recommend changes in the BCF. Teleconferences are conducted with the pharmacy consultants/specialty leaders and pharmacists representing each TRICARE region. The PEC has surveyed specialty consultants and MTF providers to obtain input on important drug classes such as COX-2 inhibitors, proton pump inhibitors, LHRH agonists, and low molecular weight heparins, but these are informal surveys instituted on a case-by-case basis. There is no formal, recognized, systematic method for MTF providers to routinely have input on formulary and contracting issues.

The Council appointed a subcommittee to explore ways to systematically obtain input from providers on formulary and contracting issues. Subcommittee member are COL Downs, LCDR Briski, and COL Davies or his designee.

12. The meeting adjourned at 1600 hours on 15 August 2001. The next meeting will be held in the Washington DC area (specific location to be determined) and is scheduled for 14 Nov 2001 at 0800. All agenda items should be submitted to the co-chairs no later than 19 October 2001.

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

LIST OF APPENDICES

Appendix A: MTF Expenditures for Drugs Included in the Advances in Medical Practice (AMP) Program

MTF Expenditures On Amp Drugs, First Nine Months Of FY 01

Drug Name*	Air Force	Army	Navy	Grand Total
Abciximab	$254,828	$216,886	$75,396	$547,110
Alpha-1-Proteinase Inhibitor			$18,228	$18,228
Becaplermin	$62,291	$94,926	$43,818	$201,035
Cyclosporine	$322,159	$235,474	$178,033	$735,666
Cyclosporine Microemulsion	$662,783	$632,102	$628,818	$1,923,703
Dornase Alfa	$238,605	$136,393	$154,692	$529,690
Epoetin Alfa	$3,074,457	$3,640,225	$1,957,694	$8,672,375
Eptifibatide	$66,227	$299,967	$179,640	$545,834
Etanercept	$1,165,366	$825,910	$499,619	$2,490,896
Factor VIIa,Recomb		$4,218		$4,218
Filgrastim	$1,071,525	$1,379,019	$809,235	$3,259,779
Gemcitabine Hcl	$168,885	$296,224	$225,954	$691,062
Glatiramer Acetate	$368,394	$180,715	$100,230	$649,339
Infliximab	$251,723	$258,436	$332,440	$842,598
Interferon Beta-1a	$1,211,255	$979,842	$496,651	$2,687,748
Interferon Beta-1b	$374,021	$512,901	$332,929	$1,219,851
Interferon Gamma-1b,Recomb.	$41,678	$65,455	$35,905	$143,037
Irinotecan Hcl	$183,078	$427,646	$232,438	$843,162
Leflunomide	$152,077	$285,243	$171,167	$608,488
Mycophenolate Mofetil	$412,354	$518,043	$219,776	$1,150,173
Mycophenolate Mofetil HCl	$919	$2,082		$3,002
Palivizumab	$1,316,843	$1,401,470	$943,150	$3,661,463
Ribavirin/Interferon A-2b	$539,000	$1,168,805	$423,249	$2,131,054
Rituximab	$284,989	$956,443	$407,289	$1,648,721
Sargramostim	$17,853	$105,341	$8,348	$131,542
Sirolimus	$33,545	$75,817	$31,191	$140,554
Tacrolimus Anhydrous	$409,332	$367,998	$226,014	$1,003,344
Temozolomide	$122,356	$95,662	$67,134	$285,152
Tirofib Hc M-Hyd/Na Chlor 0.9%	$2,745	$21,087		$23,832
Tirofiban HCl M-Hydrate	$87,199	$55,477	$19,159	$161,835
Trastuzumab	$121,671	$269,967	$26,662	$418,300
Grand Total	$13,018,156	$15,509,775	$8,844,859	$37,372,790

* Celecoxib and rofecoxib were removed from the AMP list for FY 01

Appendix B: COX-2 Inhibitor Trials (VIGOR and CLASS)

1. Cardiovascular Safety Data from the Vioxx Gastrointestinal Outcomes Research (VIGOR) Study

The 8076-patient VIGOR trial (NEJM 2000;343:1520-8) included patients with rheumatoid arthritis (RA) who were 50 years old (or 40 years old and receiving long-term glucocorticoids) and excluded patients on low-dose aspirin for cardiovascular prevention. Patients were randomized to rofecoxib 50 mg QD or naproxen 500 mg BID. The median follow-up was 9 months (range 0.5 – 13). Use of aspirin or non-study NSAIDs was not allowed.

A detailed analysis of VIGOR data concerning the occurrence of cardiovascular events is available from FDA briefing documents, available at *www.fda.gov/ohrms/dockets/ac/01/briefing/3677b2.htm*. Overall, the rate of adjudicated thrombotic cardiovascular serious adverse events per 100 patient-years was 1.67 for rofecoxib vs. 0.70 for naproxen [relative risk (RR) 2.37; 95% confidence interval (CI) 1.39-4.06; p=0.0016]. The difference in the composite measure was primarily due to a difference in the incidence of myocardial infarctions between the rofecoxib and the naproxen group. For patients identified as potential candidates for low-dose aspirin, the difference in event rates was marked: 14.29 for rofecoxib vs. 2.94 for naproxen (RR 4.89; 95% CI 1.41-16.88; p=0.0122). For patients not considered candidates for low dose aspirin, the difference in events was less marked but still statistically significant: 1.16 for rofecoxib vs. 0.62 for naproxen (relative risk 1.88; 95% CI 1.03-3.45; p=0.041).

It has been suggested that naproxen, which is relatively COX-1 selective, may have antiplatelet effects similar to aspirin. This may explain the relatively lower incidence of thrombotic events with naproxen compared to rofecoxib, but, as stated by the FDA Advisory Committee review, a direct prothrombotic effect of rofecoxib cannot be ruled out. Whether the putative effect of naproxen in reducing cardiovascular thrombotic effects in the VIGOR trial is reasonable compared to expected results with aspirin is subject to debate. There are no trials assessing the ability of naproxen to reduce cardiovascular events.

Since RA patients appear to have a higher baseline risk for cardiovascular disease than patients with osteoarthritis (OA), the RA population in VIGOR may have been more sensitive to any potential thrombogenic effect of selective COX-2 inhibition than a population predominated by OA patients. In addition, the effect may be dose-related; the 50-mg daily dose used in VIGOR is at least two times higher than doses recommended for chronic use.

The proposed prothrombotic mechanism is related to cyclooxygenase inhibition. COX-1 mediates production of thromboxane A2, which promotes vasoconstriction, platelet activation and aggregation. COX-2 mediates production of prostaglandins at inflammatory sites as well as prostacyclin (PGI2), a vasodilator and inhibitor of platelet aggregation. If COX-2 is selectively inhibited, unopposed production of thromboxane could result in an increase in CV thrombotic effects. Compensatory mechanisms are known to exist. Whether this theoretical effect applies to celecoxib is unknown, but appears plausible based on the proposed mechanism.

2. Additional Results Concerning GI Protective Effects of Celecoxib from the Celecoxib Long-term Arthritis Safety Study (CLASS)

The Celecoxib Long-term Arthritis Safety Study (CLASS) was an 8059-patient trial that compared celecoxib (400 mg BID) to diclofenac (75 mg BID) or ibuprofen (800 mg TID). Approximately 73% of patients had osteoarthritis; 27% had rheumatoid arthritis. Use of low-dose aspirin for cardiovascular prophylaxis was permitted.

The published report of the trial (JAMA 2000;284:1247-55) was limited to data obtained during the first six months of study participation, although about 35% of patients received nine months or more of treatment. According to published six-month data, the annualized absolute risk (AR) for the primary endpoint of confirmed complicated UGI events (GI bleeds, perforation, or gastric outlet obstruction) was 0.76% for celecoxib vs. 1.45% for the pooled NSAID group (RR 0.53; 95% CI 0.26-1.11; p=0.09), a non-significant difference. The difference in AR was significant when the subgroup of patients not taking aspirin was considered [0.44% for celecoxib vs. 1.27% for the pooled NSAID group (RR 0.35; 95% CI 0.14-0.98; p=0.04)]. However, there was neither a significant difference nor a discernible trend in patients taking aspirin [2.01% for celecoxib vs. 2.12% for the pooled NSAID group (RR 0.95; 95% CI not calculated; p=0.49)], a result that raises the possibility that COX-2 inhibitors may not provide a clinically relevant GI protective effect for patients on low dose aspirin.

When the entire 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 below).

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

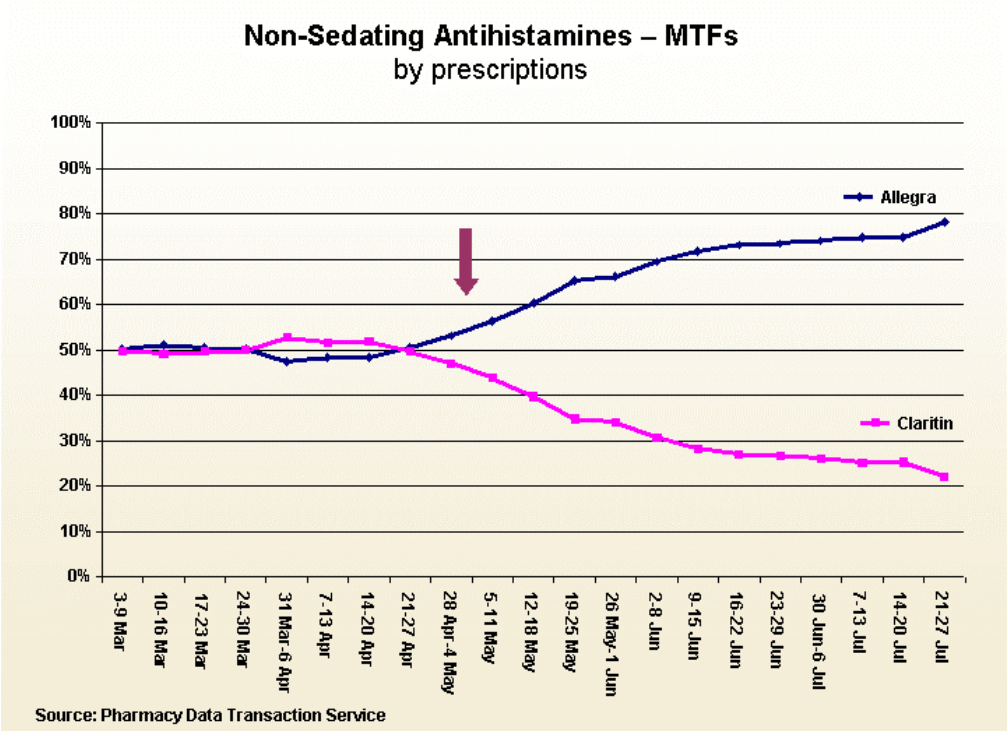
Adapted from Tables 13 and 14, Medical Officer Review for Celebrex®, available at:
www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1_03_med.doc

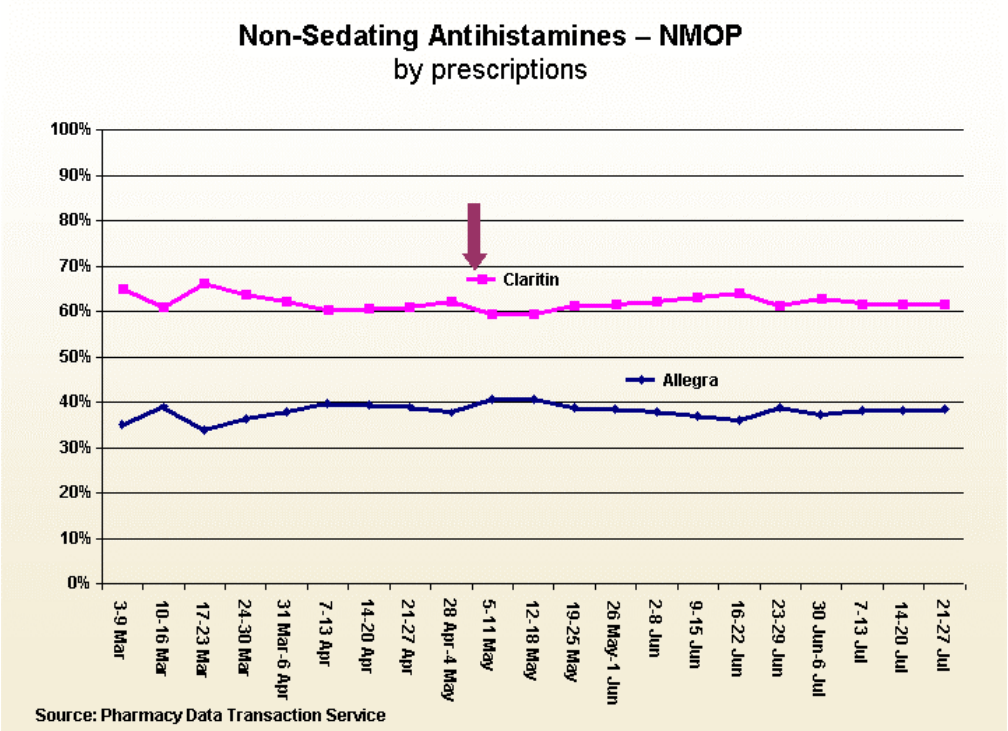
The manufacturer has suggested that this is primarily due to disproportionate dropouts secondary to GI symptoms (e.g., dyspepsia) among patients receiving comparator NSAIDs, artificially decreasing the number of patients in the NSAID group susceptible to GI adverse events. FDA reviewers raise a number of questions concerning the validity of this explanation.

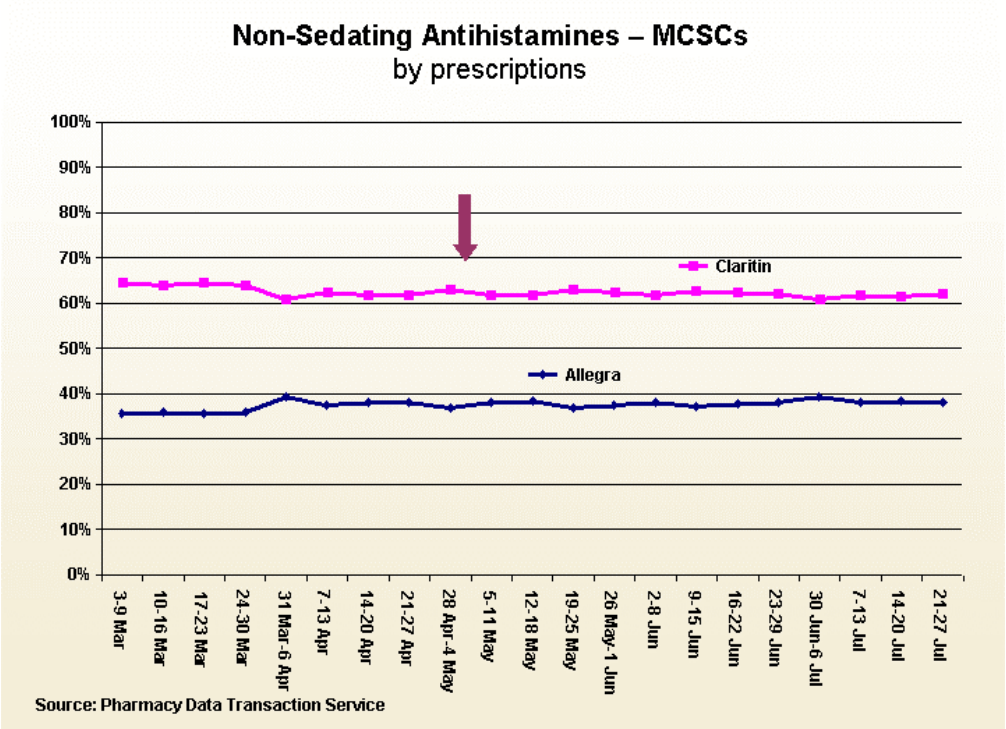
FDA briefing documents and reviews also provide separate data for the two comparator NSAIDs. All differences that were statistically significant between celecoxib and pooled NSAIDs were significant for celecoxib versus ibuprofen. The differences between celecoxib and diclofenac were not statistically significant for any of the endpoints.

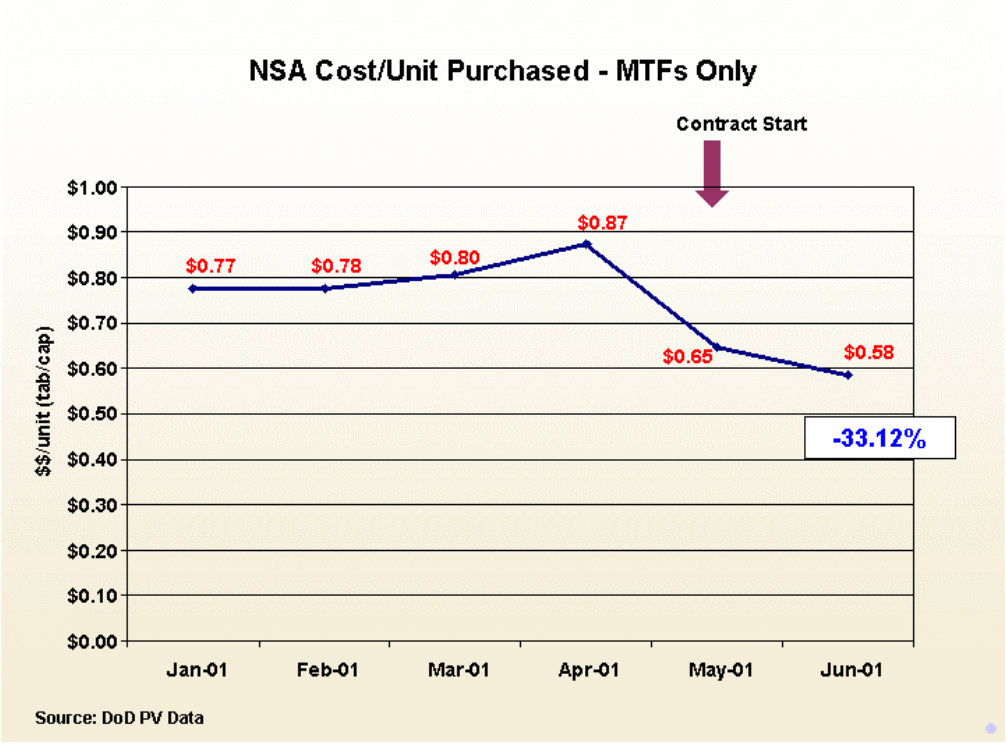
FDA briefing documents and reviews are available at *www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1.htm*.

Appendix C: Market Share and Cost Graphs for the Non-Sedating Antihistamines






Non-Sedating Antihistamines – MCSCs
by prescriptions
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Claritin
Allegra
3-9 Mar
10-16 Mar
17-23 Mar
24-30 Mar
31 Mar-6 Apr
7-13 Apr
14-20 Apr
21-27 Apr
28 Apr-4 May
5-11 May
12-18 May
19-25 May
26 May-1 Jun
2-8 Jun
9-15 Jun
16-22 Jun
23-29 Jun
30 Jun-6 Jul
7-13 Jul
14-20 Jul
21-27 Jul
Source: Pharmacy Data Transaction Service


NSA Cost/Unit Purchased - MTFs Only
Contract Start
$1.00
$0.90
$0.80
$0.70
$0.60
$0.50
$0.40
$0.30
$0.20
$0.10
$0.00
$$/unit (tab/cap)
$0.77
$0.78
$0.80
$0.87
$0.65
$0.58
-33.12%
Jan-01
Feb-01
Mar-01
Apr-01
May-01
Jun-01
Source: DoD PV Data

Department of Defense
Pharmacoeconomic Center

1750 Greeley Rd., Bldg. 4011, Rm. 217
Fort Sam Houston, TX 78234-6190

MCCS-GPE **7 JUNE 2001**

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 0900 hours on 7 June 2001, at the Uniformed Services University of the Health Sciences, Bethesda, Maryland.

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 Bill Sykora, MC	Air Force
LtCol (select) George Jones, BSC	Air Force
CAPT (select) Matt Nutaitis, MC	Navy
CDR Kevin Cook, MSC	Navy
COL Rosa Stith, MC	Army
LTC (P) Joel Schmidt, MC	Army
MAJ Brett Kelly, MS	Army
CAPT Chuck Bruner	Coast Guard
Dick Rooney	Department of Veterans Affairs
LtCol Greg Russie, BSC	Joint Readiness Clinical Advisory Board
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia (DSCP)
Ray Nan Berry	Health Net Federal Services
William Hudson	Humana, Inc
Gene Lakey	TriWest
Ron McDonald	Sierra Military Health Services
Trevor Rabie	Uniformed Services Family Health Plans (USFHP)

MEMBERS ABSENT

COL John R. Downs, MC	Air Force

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
COL Ardis Meier, BSC	Air Force Pharmacy Consultant
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
CAPT Pat Welter, MSC	Navy Bureau of Medicine & Surgery
LTC Don De Groff, MS	DoD Pharmacoeconomic Center
MAJ Cheryl Filby, MS	Defense Supply Center Philadelphia
David Chicoine	Uniformed Services Family Health Plan
Bill Chamberlain	Defense Supply Center Philadelphia
Mark Petruzzi	Merck-Medco
Shannon Rogers	Merck-Medco
Elizabeth Scaturro	Merck-Medco
Shana Trice	DoD Pharmacoeconomic Center
Vinnie Valinotti	Defense Supply Center Philadelphia
Paul Vasquez	Defense Supply Center Philadelphia
Gina Wu	Merck-Medco

3. **ADMINISTRATIVE ISSUES** – The minutes from the last meeting were accepted as written.

4. **REPORT FROM THE DOD EXECUTIVE COUNCIL MEETING** – COL Remund reviewed materials presented at the Executive Council Meeting concerning utilization and cost trends for drugs in the top six classes (by dollar expenditure) in DoD Military Treatment Facilities (MTFs) and the National Mail Order Pharmacy Program (NMOP). COL Remund also informed the committee about the award, contract provisions, and implementation of the joint VA/DoD national pharmaceutical contract for non-sedating antihistamines.

5. **IMPLEMENTATION OF FY 00 AND FY 01 NATIONAL DEFENSE AUTHORIZATION ACTS** – COL Davies briefed the Committee on the ongoing efforts to implement the pharmacy benefit provisions of the FY 00 and FY 01 National Defense Authorization Acts.

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 the Basic Core Formulary (BCF) status for 11 new drugs (see Appendix A). Additional discussion concerning the following drugs is also summarized in Appendix A: insulin glargine (Lantus; Aventis), PEG-interferon alfa 2b (PEG Intron; Schering), fluticasone/salmeterol powder for inhalation (Advair Diskus; Glaxo SmithKline), fluoxetine 90-mg capsules (Prozac Weekly; Lilly), and imatinib mesylate (Gleevec; Novartis).

7. **NON-PREFERRED/PREFERRED DRUG PAIRS IN THE NMOP** – MAJ Mickey Bellemin and Paul Vasquez (DSCP) reported that on 1 April the NMOP contractor, Merck-Medco, ceased making calls to physicians concerning all non-preferred/preferred drug pairs in the NMOP Preferred Drug Program except diltiazem. DSCP and Merck-Medco agreed to this change in order to accommodate the increased NMOP workload from the expansion of the pharmacy benefit to all beneficiaries over 65 years of age. Phone calls for diltiazem will continue because of the national contract for diltiazem extended release (Tiazac) and the high cost avoidance per attempted provider contact associated with this non-preferred/preferred drug pair.

CAPT Joe Torkildson reported a $2.8 million cumulative cost avoidance over the 22-month duration of the NMOP Preferred Drug Program (see Appendix B). COL Remund commented that the committee should continue to monitor market shares in classes in which a non-preferred/preferred drug pair existed in order to assess the true effect of these interventions and the potential effect of similar interventions in the future.

8. PRIOR AUTHORIZATIONS

A. *Cost avoidance from NMOP prior authorizations (PAs)* – Shana Trice (PEC) 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.

PA Cost Avoidance per New Prescription Submitted to the NMOP*

Drug	3rd Quarter FY 00	4th Quarter FY 00	1st Quarter FY 01	2nd Quarter FY 01
Sildenafil	$13.60	$26.46	Not calculated**	Not calculated**
COX-2 inhibitors	$11.66	$18.56	$10.95	$8.74
Etanercept	$327.20	$111.86	$7.89	$76.96

* 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.

** The PEC is working with Merck Medco and DSCP to revise the PA cost avoidance model to account for prior authorization of refill prescriptions.

- *Etanercept* – The progressive decline in the cost avoidance for the etanercept PA in the NMOP noted at the last meeting appears to have reversed (see table). However, considering the high cost of etanercept, the low number of prescriptions, and the even lower number of prescriptions that go through the PA process, the analysis is likely to be extremely sensitive to small changes in the number of prescriptions that are not filled because they do not meet PA criteria. The analysis of cost avoidance due to the etanercept PA in the retail network discussed at the last meeting has not yet been completed. The committee did not take any action concerning the etanercept PA.

B. *Temporary lapse in the NMOP PA program* – Paul Vasquez (DSCP) reported that the NMOP PA program was suspended from mid April 01 to early May 01 to accommodate large increases in NMOP workload due to the expansion of the pharmacy benefit to all beneficiaries over 65 years of age.

C. *Utilization of the NMOP and retail network pharmacies for drugs subject to PA* – The committee discussed the possibility of using data from the Pharmacy Data Transaction Service (PDTS) to analyze the extent to which patients who are denied prescriptions for COX-2 inhibitors in the NMOP subsequently fill these prescriptions at retail network pharmacies. The COX-2 inhibitor PA was withdrawn in the retail network in Aug 00 because federal regulations governing TRICARE currently allow prior authorizations to be applied in the retail pharmacy

networks only for clinical considerations (appropriateness of therapy), and not for cost-effectiveness considerations.

Bill Hudson (Humana) presented longitudinal data concerning utilization and costs of COX-2 inhibitors, brand name nonsteroidal anti-inflammatory drugs (NSAIDs) and generic NSAIDs in Regions 3 and 4. He reported that utilization of COX-2 inhibitors, which had decreased when the COX-2 inhibitor PA had been put into place, essentially doubled when the COX-2 inhibitor PA was discontinued.

The number of patients who opt to fill COX-2 inhibitor prescriptions in retail network pharmacies instead of the NMOP due to the presence of the COX-2 inhibitor PA is unknown. Prescriptions filled at the NMOP are less costly to DoD than those filled in the retail network. In addition, it is likely that some patients who opt to fill one prescription in the retail network rather than the NMOP will decide to fill all their prescriptions in the retail network. The committee requested that the PEC utilize data from PDTS to analyze the shift of patients from NMOP to the retail network.

C. *Antifungals for onychomycosis* – Ciclopirox topical solution (Penlac Nail Lacquer) was added to the existing NMOP PA for antifungals for onychomycosis as of 10 May 01. No problems with NMOP implementation were reported.

Bill Hudson (Humana) expressed concern about combination therapy with oral antifungals and ciclopirox being prescribed by a small number of providers. It is doubtful that this combination increases the effectiveness of onychomycosis treatment by any clinically significant degree. Product labeling for ciclopirox recommends against concurrent therapy with oral antifungals since it is not known whether ciclopirox interferes with the action of the oral antifungals. Because ciclopirox requires regular visits to remove infected nail material, use of the combination not only increases medication cost but may also increase the total cost of therapy. The committee requested more information about the incidence of combination therapy.

D. *Revision of PA forms* – Changes to clinical rationale language for the COX-2 inhibitors due to the CLASS study are in progress. The committee requested that clinical rationale language for the antifungals for onychomycosis to be changed to reflect recent safety announcements by the Food and Drug Administration (FDA) concerning terbinafine and itraconazole.

9. STATUS OF LOW MOLECULAR WEIGHT HEPARINS (LMWHs) IN THE NMOP AND RETAIL NETWORK – CAPT Torkildson reported on the PEC's survey of providers concerning the necessity to have the LMWHs available through the NMOP. While most providers did not feel this to be necessary, the obstetricians surveyed agreed that their patients were prescribed LMWH therapy for a long enough period of time to make acquiring the drug from the NMOP a viable option. While the volume of prescriptions is expected to be low, the committee agreed that there is no reason to not have low molecular heparins designed for self-administration available through the NMOP for those patients who might benefit. The committee added LMWHs (dalteparin, enoxaparin, and tinzaparin) to the NMOP formulary. The low molecular weight heparinoid, danaparoid, was not added because it is indicated for intravenous administration only and is unlikely to be administered as an outpatient medication.

10. REVIEW OF INJECTABLE MEDICATIONS AVAILABLE THROUGH THE NMOP - The committee clarified that the potential for self-administration is only one of the factors for considering drugs for the NMOP Covered Injectables List. Other factors include the feasibility of

dispensing the medications through mail order (Merck-Medco's mail order facilities are not set up to handle sterile compounding of parenteral products) and the relative likelihood that the medications will be needed on an outpatient basis.

One of the MCSC pharmacy directors requested removal of Zoladex from the NMOP Covered Injectables list, since it is an implant that requires an office visit and insertion under sterile conditions. It was pointed out that Lupron, although administered as an intramuscular injection rather than implanted subcutaneously, is in most cases also not suitable for self-administration. The committee requested the PEC to review the NMOP Covered Injectables list to identify items not designed for self-administration or commonly used in an outpatient setting and review the current utilization of these medications through the NMOP. The committee did not change the availability of Zoladex through the NMOP at this time, pending results of the review.

11. **CONTROLLED DISTRIBUTION OF ETANERCEPT (ENBREL) –** Since MTF pharmacies, unlike retail pharmacies, are not required to submit patient enrollment numbers to obtain etanercept, DoD beneficiaries can obtain etanercept from MTF pharmacies even if they did not enroll with Immunex. However, unenrolled patients may experience problems if they need to obtain etanercept from a source other than an MTF pharmacy. A process has been established for patients not enrolled with the manufacturer who have been receiving etanercept from a MTF and who wish to obtain their medication through the retail network, or who have separated from the military, to obtain enrollment numbers and receive etanercept through the NMOP or a retail network pharmacy. Patients who have not previously received etanercept (new starts) are subject to the same waiting list procedures as civilian patients. LTC De Groff reported that a letter addressing these procedures has been sent to the field by the pharmacy consultants/specialty leaders. A copy of the letter is available as Appendix D.

12. **CONTROLLED DISTRIBUTION OF DOFETILIDE (TIKOSYN) –** Because of specialized educational requirements mandated by the FDA, dofetilide is only available for outpatient use through Stadtlander's Pharmacy/CVS Procare (which is a non-network pharmacy for DoD beneficiaries). COL Davies reported that the biggest problem is that prime patients are being forced to pay the copay for a non-network pharmacy. He reported that there is a potential for developing a new payment mechanism to handle not just dofetilide, but also the increasing number of drugs with unique distribution systems. Efforts to establish such a payment mechanism are in progress.

13. **ADJOURNMENT –** The meeting adjourned at 1400 hours. The next meeting will be held at Ft Sam Houston, TX and is tentatively scheduled for 16 Aug 01 at 0800. All agenda items should be submitted to the co-chairs no later than 20 Jul 01.

<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 or retail network formulary restrictions**	**BCF Status**
Ziprasidone capsules (Geodon; Pfizer)	5 Feb 01; atypical antipsychotic for the treatment of schizophrenia. Labeling for ziprasidone specifically notes that: "When deciding among the alternative treatments available for this condition, the prescriber should consider the finding of ziprasidone's greater capacity to prolong the QT/QTc interval compared to several other antipsychotic drugs." It is not known whether ziprasidone will cause torsade de pointes.	Added to NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **BCF drugs in this class:** antipsychotics: haloperidol oral; no atypical antipsychotics
Galantamine tablets (Reminyl; Johnson & Johnson)	23 Feb 01; acetylcholinesterase inhibitor; indicated for the treatment of mild to moderate dementia of Alzheimer's disease	Added to NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **BCF drugs in this class**: None
Bimatoprost ophthalmic solution, 0.03% (Lumigan; Allergan)	16 Mar 01; synthetic prostamide (prostaglandin analog); indicated for reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension; should be used in patients who cannot tolerate or have failed treatment with other IOP-lowering medications	Added to NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **BCF drugs in this class:** Ophthalmic agents for glaucoma: timolol, brimonidine, and pilocarpine ophthalmic solutions; no prostaglandin analogs
Travoprost ophthalmic solution, 0.004% (Travatan; Alcon)	16 Mar 01; synthetic prostaglandin analog; indicated for reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension; should be used in patients who cannot tolerate or have failed treatment with other IOP-lowering medications	Added to NMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **BCF drugs in this class:** Ophthalmic agents for glaucoma: timolol, brimonidine, and pilocarpine ophthalmic solutions; no prostaglandin analogs

Generic name (Trade name; manufacturer)	FDA approval date, drug class, FDA-approved indication	NMOP Formulary Status	NMOP or retail network formulary restrictions	BCF Status
Insulin glargine [rDNA origin] injection (Lantus; Aventis)	20 Apr 00 (launched 21 May 01); long-acting (basal) insulin; indicated for once daily SQ administration at bedtime for treating adult and pediatric patients with type 1 diabetes mellitus, or adult patients with type 2 diabetes mellitus who require basal (long-acting) insulin for the control of hyperglycemia. **Note:** Insulin glargine is a clear solution that should not be mixed with other insulin products; use of insulin glargine does not eliminate the need for mealtime coverage.	Added to NMOP Formulary **Note**: The NMOP Covered Injectables list includes all forms of insulin and insulin analog products (i.e., Humalog)	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **BCF drugs in this class:** Human insulin [rDNA origin} NPH, regular, 70/30 (Novolin brand only). There is a DoD/VA single source contract for the 10 mL bottles of these products (the contract also includes human lente insulin). The contract does not affect formulary status of other insulin products.
Comments about insulin glargine: The committee agreed that, while insulin glargine represents an advance in diabetes therapy and may be rapidly adopted by clinicians, it is too early to add it to the BCF. The PEC will monitor usage and will bring the item back to the committee for reconsideration if usage and demand for the product increase markedly and when clinicians have had a chance to become familiar with the product. The true potential advantage of basal insulin may only be realized when intranasal insulin becomes available, since this combination may allow even insulin dependent diabetics to limit subcutaneous injections to one daily.				
PEG-interferon alfa-2b powder for SC injection (PEG-Intron; Schering)	19 Jan 01; interferon product; indicated as once-weekly monotherapy of chronic hepatitis C in patients not previously treated with interferon alpha who have compensated liver disease, and who are at least 18 years old	Added to the NMOP Formulary **Note**: Interferon alfa products (Infergen, Roferon-A, Intron A) and combination interferon alfa/ribavirin (Rebetron) are on NMOP Covered Injectables list	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF **BCF drugs in this class:** None
Comments about Hepatitis C treatment: The VA representative, Mr. Dick Rooney, reported on the VA Chicago Health System's protocol for treatment of hepatitis C with ribavirin/interferon alfa 2b (Rebetron). Approximately 70% of patient with hepatitis C in North America are infected with genotype 1, which is less likely to respond to interferon treatment than genotypes 2 or 3. The VA performs a genotype test (which costs approximately $70) after the patient and provider have reached intention to treat. Patients with genotype 1 are then treated for one year, compared to six months for other genotypes. This both prevents unnecessary exposure to treatment that is unlikely to result in benefit and is cost-effective (cost savings of approximately $15,800 per 10 patients tested, not including avoidance of drug side effects and reduced provider visits and laboratory monitoring).				

Generic name (Trade name; manufacturer)	FDA approval date, drug class, FDA-approved indication	NMOP Formulary Status	NMOP or retail network formulary restrictions	BCF Status
Fluticasone / salmeterol powder for inhalation **100/50, 250/50, and 500/50 mcg per inhalation** (Advair Diskus; Glaxo SmithKline)	18 Aug 00; combination product containing an oral inhaled corticosteroid and a long-acting beta agonist; indicated for the long-term, twice-daily, maintenance treatment of asthma in patients 12 years of age and older. Advair is not indicated for the relief of acute bronchospasm.	Added to NMOP Formulary	**Quantity Limits** 1 inhaler (60 blisters) per 30 days (retail), 3 inhalers (180 blisters) per 90 days (NMOP) **Prior Authorization** No	Not added to BCF **BCF drugs in this class:** No other oral inhaled corticosteroid/beta agonist combination products exist; both fluticasone and salmeterol oral inhalers are on the BCF
Comments about fluticasone/salmeterol oral inhaler: The committee agreed that there is no evidence to support a clinically significant advantage (in terms of improved safety or efficacy) for the combination product compared to the two component products given separately. The combination product may be more convenient than two individual inhalers and may result in better compliance with therapy. On the other hand, the fixed dose combinations may make titration (including temporary increases in fluticasone dose during peak seasons, respiratory infections, etc.) more difficult. Advair is a dry powder Diskus device, which is substantially different from metered dose inhaler devices. Most use of fluticasone products in DoD is for the metered dose inhaled product, with minimal use of the currently available Flovent Diskus device. There is no price advantage to Advair compared to fluticasone and salmeterol given separately, although there may be cost efficiencies to MTF pharmacies (fewer prescriptions to fill) and patients (one less copay at NMOP or retail). Patent protection on fluticasone, the oral inhaled corticosteroid with the largest market share in DoD, is expected to expire in the latter part of 2003, although an "A-rated" generically substitutable product is unlikely due to environmental restrictions on production of chlorofluorocarbons (CFCs). The committee decided not to add this combination product to the BCF. The PEC will continue to monitor usage in this rapidly changing drug class.				
Formoterol fumarate powder for inhalation (Foradil; Novartis)	16 Feb 01; long-acting beta agonist; indicated for long-term, twice daily (morning and evening) administration in the maintenance treatment of asthma and in the prevention of bronchospasm in adults and children 5 years of age and older with reversible obstructive airways disease, including patients with symptoms of nocturnal asthma, who require regular treatment with inhaled, short-acting, beta2-agonists. It is not indicated for patients whose asthma can be managed by occasional use of a short-acting beta2-agonist. **Note:** formoterol has a more rapid onset of action than salmeterol (2-3 minutes vs. 10-15 minutes), previously the only available long-acting oral inhaled beta agonist. However, it is NOT a substitute for albuterol as a quick-relief medication.	Added to NMOP Formulary	**Quantity Limits** 1 inhaler (60 capsules) per 30 days (retail), 3 inhalers (180 capsules) per 90 days (NMOP) **Prior Authorization** No	Not added to the BCF **BCF drugs in this class:** salmeterol oral inhaler

Generic name (Trade name; manufacturer)	FDA approval date, drug class, FDA-approved indication	NMOP Formulary Status	NMOP or retail network formulary restrictions	BCF Status
Fluoxetine HCl 90-mg capsule (Prozac Weekly; Lilly)	26 Feb 01; selective serotonin reuptake inhibitor; indicated for the maintenance treatment of depression after an initial antidepressant response is obtained with once daily fluoxetine	Added to NMOP Formulary	**Quantity Limits** 4 capsules (one blister pack) per 30 days (retail); 12 capsules (3 blister packs) per 90 days (NMOP) **Prior Authorization** No	Excluded from BCF listing for fluoxetine. MTFs are not required to add Prozac Weekly to their formularies, but may do so if they so desire. **BCF drugs in this class:** citalopram, fluoxetine (excludes Sarafem), paroxetine, sertraline
Comments about fluoxetine 90-mg once-weekly capsule: Weekly administration of fluoxetine may represent a convenience advantage over once daily dosing, although this remains to be proven. The implications of once weekly dosing of medications for patient adherence to therapy are unknown. Plasma concentrations fluctuate to a much greater degree with once weekly dosing; the effect of patients missing once weekly doses or taking them a few days late may effectively equate to interruptions in therapy, even with the long half-life of fluoxetine. The pharmacokinetic effects, clinical consequences, and adverse effects associated with once weekly doses greater than 90 mg are unknown. The 90-mg capsule appears to be associated with more diarrhea than the 20-mg capsule, despite its delayed release formulation. The weekly formulation does not appear to be any more effective, and may be less effective, than once daily dosing. It is indicated only for maintenance treatment of depression. Prozac Weekly 90 mg once weekly costs less per month than Prozac 20 mg once daily. However, impending generic availability of fluoxetine (expected in Aug 01) and anticipated price decreases render this cost difference irrelevant, even without considering the uncertain clinical utility of this formulation of fluoxetine.				
Esomepra-zole (Nexium; AstraZeneca)	20 Feb 01; proton pump inhibitor (PPI); indicated for 1) short-term healing of confirmed erosive esophagits; 2) maintenance of healing of erosive esophagitis; 3) treatment of symptomatic gastroesophageal reflux disease (GERD); and 4) combination therapy with clarithromycin and amoxicillin for the eradication of Helicobacter pylori in patients with duodenal ulcer disease or a history of duodenal ulcer disease	Excluded from the NMOP Formulary as a non-contract drug. Prescriptions for esome-prazole may be filled through the NMOP only if documented medical necessity is established.	**Quantity Limits** General rule applies **Prior Authorization** No	Not added to the BCF. The PPI drug class is closed on the BCF. MTFs are required to have the contract agent (omeprazole) on their formularies and may not have any non-contract PPIs, including esomeprazole, on their formularies. Prescriptions for esomeprazole may be filled at MTFs only if documented medical necessity is established. **BCF drugs in this class:** omeprazole

Generic name (Trade name; manufacturer)	FDA approval date, drug class, FDA-approved indication	NMOP Formulary Status	NMOP or retail network formulary restrictions	BCF Status
Imatinib mesylate (Gleevec; Novartis)	10 May 01 (accelerated approval); protein-tyrosine kinase inhibitor (new drug class); oral once daily medication with a relatively favorable adverse effect profile; indicated for the treatment of patients with chronic myeloid leukemia (CML) in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy	Added to the NMOP Formulary	**Quantity Limits** Limited to 45 days supply in the NMOP; general rule applies in the retail network **Prior Authorization** No, monitor usage	Not added to the BCF **BCF drugs in this class:** None (there are no other drugs in this class). The only antineoplastic agents on the BCF are tamoxifen and methotrexate.

Comments about imatinib mesylate: This drug is an entirely novel antineoplastic agent. Imatinib inhibits the abnormal protein-tyrosine kinase that results from the Bcr-Abl gene rearrangement characteristic of chronic myelogenous leukemia (CML). This mechanism of action suggests that it would only be active against tumors that express this abnormal protein; however, it also has some activity against other protein-tyrosine kinases, some of which are constitutively expressed by other tumor types. It is currently approved only for use in CML; its use should be confined to those patients who are Philadelphia chromosome positive, since this indicates the presence of the Bcr-Abl gene.

Imatinib also has activity against the c-kit protein-tyrosine kinase that is constitutively expressed in at least 70% of small cell lung cancers and in virtually all gastrointestinal stromal tumors. *In vitro* studies have suggested that imatinib may have activity against small cell lung cancer, while a recent case report described a patient with a gastrointestinal stromal tumor who experienced a good partial response to therapy following treatment with imatinib that was maintained for at least 11 months. Imatinib has also demonstrated activity against the protein-tyrosine kinase activated by platelet-derived growth factor (PDGF) receptor that is activated abnormally in many brain tumors, No data are currently available that suggest efficacy in treating this condition. Animal studies suggest that imatinib may decrease the rate of restenosis of coronary arteries following angioplasty due to its inhibition of the protein-tyrosine kinase that is normally activated by PDGF following this procedure. There are therefore several additional conditions for which there are very limited data suggesting the possibility of benefit.

Imatinib capsules are dosed once daily, and are relatively well tolerated in comparison to other chemotherapeutic regimens. The monthly cost of therapy based on FSS prices ranges from approximately $1,500 (chronic CML) to $2,200 (treatment of CML in accelerated phase or blast crisis). Because of the limited scope of the available published clinical trials, the optimal duration of treatment remains undefined.

Members of the committee expressed concern over several factors that increase the potential for this product to be used for other than FDA approved indications. These include: the publicity in the lay press surrounding imatinib's release, the possibility that this drug may have efficacy in other malignancies, and the pressure from patients with other malignancies who have failed conventional therapy and have few or no remaining alternatives for treatment. 32 CFR 199.4(g)(15) states in part: "CHAMPUS can also consider coverage of unlabeled or off-label uses of drugs that are Food and Drug Administration (FDA) approved drugs that are used for indications or treatments not included in the approved labeling. Approval for reimbursement of unlabeled or off-label uses requires review for medical necessity, and also requires demonstrations from medical literature, national organizations, or technology assessment bodies that the unlabeled or off-label used of the drug is safe, effective and in accordance with nationally accepted standards of practice in the medical community."

Concern was also expressed that unmonitored use of imatinib might result in a delay in appreciating its value in treating other conditions. The committee discussed the possibility of instituting a prior authorization for this medication in the NMOP and retail network in order to minimize inappropriate use while allowing identification of additional indications. The proposed wording of the requirement for authorization was stated as, "treatment of an FDA-approved indication, or enrollment in an NCI-approved clinical trial". However, the committee was then reminded that 32 CFR 199.4 also excludes coverage for "services and supplies provided as a part of or under a scientific or medical study, grant, or research program." It was pointed out that the lack of a prior authorization does not prevent MCSC Utilization Management Programs from ensuring that prescribed therapy complies with TRICARE rules. The Committee appreciated that strict application of TRICARE rules will likely engender strong objections from patients and prescribers in this situation. Also, with over 350 new oncology drugs currently undergoing clinical trials, it was understood that this question would likely surface repeatedly in the future. The Committee felt that input from a higher level within TMA would be valuable in assisting them in determining how best to deal with this issue.

The committee approved placing imatinib on the NMOP formulary without a requirement for prior authorization. A quantity limit of a 45-day supply was established to minimize waste without overly burdening patients. Without a PA, the NMOP will not collect data on diagnoses of patients prescribed the drug. The PEC will monitor usage and report at the next meeting.

APPENDIX B: CUMULATIVE SUMMARY OF COST AVOIDANCE ASSOCIATED WITH THE NATIONAL MAIL ORDER PHARMACY (NMOP) PREFERRED DRUG PROGRAM

Program Summary

- Program started in June 1999 with 8 preferred/non-preferred groups and ended 31 Mar 01 as a result of increased prescription volume related to expansion of the DoD pharmacy benefit to allow all DoD beneficiaries 65 years of age or older access to the NMOP and retail network. Calls will continue for diltiazem due to the existence of the national contract for Adalat CC.
- During these 22 months, the program resulted in a total cost-avoidance of $2,841,647. A total of 31,574 attempted prescriber contacts were made to request switches from non-preferred drugs to preferred alternatives. The estimated cost-avoidance per attempted provider contact was $90.

Cumulative Table: Summary of Switch Rates and Estimated Cost Avoidances Jun 99 – Mar 01*

Non-Preferred Drug	Preferred Drug	Switch Rate	Estimated Cost Avoidance	Total Number of Attempted Provider Contacts*	Estimated Cost Avoidance per Attempted Provider Contact**	Annualized Estimated Cost Avoidance
Cardizem CD Dilacor XR, Diltia XT, Diltiazem XR	**Tiazac**	69%	$905,784	6392	$142	$494,064
Procardia XL[1]	**Adalat CC**	51%	$417,508	2097	$199	$227,732
Lodine XL, Relafen, Voltaren XR, DayPro, Naprelan	**Generic NSAIDs**	30%	$724,985	7791	$93	$395,446
H2 Blockers[2]	**Generic Ranitidine**	40%	$437,715	3749	$117	$238,754
Enalapril (Vasotec)[3]	**Zestril**	48%	$141,304	2741	$52	$77,075
Famvir, Valtrex[4]	**Acyclovir**	23%	$11,081	1670	$7	$6,044
Pletal[5]	**Pentoxifylline**	12%	$3,424	280	$12	$1,868
Ditropan XL, Detrol	**Generic oxybutynin**	29%	$199,846	6854	$29	$109,007
		Total	$2,841,647	31,574	$90	$1,549,990

* Assumes that each new prescription received for a non-preferred drug resulted in one attempted provider contact.

** Calculated as the total cost avoidance Oct 00 – Mar 01 divided by the total number of attempted provider contacts made for non-preferred drugs in this class during the same period.

1. Calls for Procardia XL diminished significantly (from 135 per month in Jun 00 to 7 per month in Dec 00), due to the introduction of generic equivalents for some strengths of Procardia XL. Calls for Procardia XL were discontinued as generic equivalents became available.
2. Implemented Dec 99
3 Implemented Feb 00. Vasotec was removed from the list of non-preferred drugs when a generic equivalent became available at a competitive price in Oct 00.
4. At the May 00 meeting, the committee changed the criteria for Famvir and Valtrex so that calls would be made only for prescriptions written for chronic use (> 30 day supply). This change took effect 1 July 00.
5. Implemented Feb 00. Removed from the list of non-preferred drugs at the Aug 00 meeting (effective Sep 00), due to a low switch rate.

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) Fluocinonide 0.05% cream

   B. *Changes and clarifications to the BCF*

      1) The BCF listing for digoxin oral was changed to remove the specific brand designation for brand name Lanoxin.
      2) The BCF listing for doxycycline oral was clarified to exclude doxycycline 20-mg capsules (Periostat).
      3) The BCF listing for methylphenidate oral was clarified to exclude Metadate CD.
      4) The BCF listing for triamcinolone acetonide 0.1% topical was clarified to specify triamcinolone 0.1% cream.

2. **NMOP FORMULARY CHANGES**

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

      1) Low Molecular Weight Heparins (dalteparin, enoxaparin, tinzaparin)
      2) Ziprasidone (Geodon; Pfizer)
      3) Galantamine (Reminyl; Johnson & Johnson)
      4) Bimatoprost ophthalmic solution, 0.03% (Lumigan; Allergan)
      5) Travoprost ophthalmic solution, 0.004% (Travatan; Alcon)
      6) Insulin glargine [rDNA origin] injection (Lantus; Aventis)
      7) PEG-interferon alfa-2b powder for SC injection (PEG-Intron; Schering)
      8) Fluticasone/salmeterol powder for inhalation (Advair Diskus; Glaxo SmithKline)
      9) Formoterol fumarate powder for inhalation (Foradil; Novartis)
      10) Fluoxetine hydrochloride 90-mg capsule (Prozac Weekly; Lilly)
      11) Imatinib mesylate (STI-571) (Gleevec; Novartis)

   B. *Exclusions from the NMOP Formulary*

      1) Esomeprazole (Nexium; Astra Zeneca)

   C. *Changes to the NMOP Preferred Drug Program*

      1) The NMOP Preferred Drug Program was discontinued 31 Mar 01. Calls requesting switches for non-contracted brands of diltiazem extended release (e.g., Cardizem CD, Dilacor XR, Diltia XT, Cartia XT, and generics) to the contract agent (Tiazac) will continue.

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

   A. Fluticasone/salmeterol powder for inhalation (Advair Diskus; Glaxo SmithKline) - 1 inhaler (60 blisters) per 30 days (retail), 3 inhalers (180 blisters) per 90 days (NMOP)
   B. Formoterol fumarate powder for inhalation (Foradil; Novartis) - 1 inhaler (60 capsules) per 30 days (retail), 3 inhalers (180 capsules) per 90 days (NMOP)
   C. Fluoxetine hydrochloride 90-mg capsule (Prozac Weekly; Lilly) - 4 capsules (one blister pack) per 30 days (retail); 12 capsules (3 blister packs) per 90 days (NMOP)
   D. Imatinib mesylate (STI-571) (Gleevec; Novartis) - Limited to 45 days supply in the NMOP; general rule applies in the retail network

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

APPENDIX D: ENBREL ENROLLMENT LETTER

ENBREL ENROLLMENT PROCESS

The following procedures should be used when dealing with patients on Enbrel (etanercept) in the Department of Defense medical treatment system. These procedures will remain in place until the DOD is notified by Immunex and/or Wyeth that they have changed. These procedures are based on current inventories of product.

1. Patients who were on Enbrel therapy before January 1, 2001 who enrolled in the Enbrel Enrollment Program and received a registration number will keep this number in the Immunex system. These patients will not be disenrolled by Immunex, although their number will remain "inactive" if they are receiving product through an MTF pharmacy or the NMOP mail order system. In some instances the NMOP system may require this number. If this is the case, Immunex will activate the number. This number will be used if the patient is receiving product through the retail pharmacy network program.

2. Patients who are receiving Enbrel therapy from a MTF pharmacy who are required to move for military or personal reasons (i.e. PCS, TDY assignments, relocations) and who prefer to continue to receive product from either an MTF pharmacy or the NMOP mail order system should notify the pharmacy from where they are moving. This pharmacy should contact Warren H. Yeager, R.Ph., National Account Manager-Federal Government, Wyeth-Ayerst Labs @ 1-888-685-5961 ext. 76924 and notify him of the new location of the patient. This will keep track of product at the different delivery systems throughout the DOD.

3. DOD patients who choose the retail pharmacy network option for obtaining Enbrel.

   - If these patients have already enrolled in the program and have a registration number and have been receiving product there will be no change in the process.

   - Because of the portability of the prescription in the DOD, if an Enbrel patient chooses to change from an MTF or NMOP to the retail option to have their script filled and does not have an enrollment number, the dispensing pharmacist will have to "opt out" of the confirmation process. The term "opt out" is recognized by the retail pharmacy network and is put in place to have the retail pharmacy contact HDS McKesson (1-888-436-2735) when this situation presents itself. HDS McKesson personnel are aware of this scenario. If the patient has an "inactive" number, this number will be activated by HDS McKesson and the patient will receive the medication. If the patient does not have a number, HDS McKesson will assign a number and the patient will receive the medication.

4. Patients who transfer from the DoD to the private sector due to separation.

   - Because these patients are already "accounted for" in the overall enrollment process they will be given an active enrollment number at the time of separation. The patient will need to call HDS McKesson @ 1-888-436-2735 and identify themselves as an existing patient transferring from DoD to the private sector due to release from Active military service. HDS McKesson will verify DoD eligibility and assign an enrollment number that will allow the patient to continue to receive the medication. HDS McKesson can verify the patient's DoD eligibility and medication history by calling the PDTS CSSC @ 1-800-600-9332, press #1, then select option #1 a second time.

5. Wait list procedures for adding new patients to the DOD program.

   - Patients will follow the same procedures as patients in the civilian community. They will need to call 1-888-436-2735(1-888-4ENBREL). They will be placed on the waiting list and given a "inactive" registration number.

Department of Defense
Pharmacoeconomic Center

1750 Greeley Rd., Bldg. 4011, Rm. 217
Fort Sam Houston, TX 78234-6190

MCCS-GPE **6 June 2001**

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 1215 hours on 6 June 2001 and from 0800 to 0900 hours on 7 Jun 2001, at the Uniformed Services University of the Health Sciences, Bethesda, MD. The DoD P&T Executive Council is responsible for performing certain inherently governmental functions relevant to the DoD pharmacy benefits program. The Council focuses primarily on issues related to the Basic Core Formulary (BCF), national pharmaceutical contracts, and blanket purchase agreements. The DoD P&T Executive Council is comprised of federal employees who are members of the DoD P&T Committee.

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
LtCol (select) 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, MS	Army
CAPT Chuck Bruner	Coast Guard
Dick Rooney	Department of Veterans Affairs
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia
LtCol Greg Russie, BSC	Joint Readiness Clinical Advisory Board representative

MEMBERS ABSENT

COL Bill Sykora, MC	Air Force
COL Rosa Stith, MC	Army

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TRICARE Management Activity
COL Mike Heath, MS	Army Pharmacy Consultant; Chair, DoD Pharmacy Board of Directors
COL Ardis Meier, BSC	Air Force Pharmacy Consultant
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
CAPT Pat Welter, MSC	Navy Bureau of Medicine & Surgery
LTC Don De Groff, MS	DoD Pharmacoeconomic Center
MAJ Cheryl Filby, MS	Defense Supply Center Philadelphia
MAJ Barbara Roach, MC (by teleconference)	DoD Pharmacoeconomic Center
LT David Hardy, MSC	TRICARE Management Activity
Angela Allerman (by teleconference)	DoD Pharmacoeconomic Center
Howard Altschwager	Deputy General Counsel, TRICARE Management Activity
Jonathan Blaker	TRICARE Management Activity
Bill Chamberlain	Defense Supply Center Philadelphia
Shana Trice	DoD Pharmacoeconomic Center
Vincent Valinotti	Defense Supply Center Philadelphia
Paul Vasquez	Defense Supply Center Philadelphia

3. REVIEW MINUTES OF LAST MEETING

The minutes were approved as written.

4. ADVANCES IN MEDICAL PRACTICE (AMP) PROGRAM

All AMP funds remain "on hold" at TMA due to funding shortfalls in the Defense Health Program. If AMP funds are released, the PEC is prepared to provide usage and cost data to facilitate reimbursement of MTFs for expenditures on AMP drugs. Based on prime vendor data, MTFs spent $25,831,626 on AMP drugs during the first six months of FY 01 (see Appendix A).

5. REVIEW OF COX-2 INHIBITORS

The committee reviewed usage and cost data for COX-2 selective nonsteroidal anti-inflammatory drugs ("COX-2 inhibitors") and other nonsteroidal anti-inflammatory drugs (NSAIDs):

- Data from the Pharmacy Data Transaction Service from 1 Apr 01 to 25 May 01 indicated that market share for COX-2 inhibitors in MTFs has increased to 14% of all prescriptions for NSAIDs. Market shares for COX-2 inhibitors in the retail networks and the NMOP were 58% and 74% respectively (see table following).

	MTFs	MCSC retail network	NMOP
Number of prescriptions and percent of prescriptions for NSAIDs			
COX-2 inhibitors	56,822 (14%)	72,654 (58%)	25,525 (74%)
Traditional NSAIDs	345,621 (86%)	53,245 (42%)	8,853 (26%)
Total number of prescriptions for NSAIDs	402,443	125,899	34,378
Number of patients and percent of patients using NSAIDs			
COX-2 inhibitors	44,963 (13%)	54,151 (58%)	23,454 (75%)
Traditional NSAIDs	289,313 (87%)	39,946 (42%)	7,907 (25%)
Total number of patients using NSAIDs	334,276	94,097	31,361

Note: time period is 4/1/01 through 5/25/01; data from the Pharmacy Data Transaction Service Customer Service Support Center

- The PDTS data are consistent with data from the Uniformed Services Prescription Database (USPD), which indicated a 14% market share (by prescription volume) for COX-2 inhibitors at MTFs as of March 2001. TRICARE region market shares for COX-2 inhibitors ranged from less than 5% to more than 20%.
- According to prime vendor data, MTFs spent $19.1 million on NSAIDs during the first 6 months of FY 01, which is 84% more than the $10.4 million spent during the first 6 months of FY 00. The average unit cost of NSAIDs purchased by MTFs rose from $0.06 in October 98 to $0.22 in March 01.

The Council agreed that management of the COX-2 inhibitors should ideally focus on two issues:

- COX-2 inhibitor therapy should be targeted accurately and efficiently to those patients at greatest risk for GI adverse events
- DoD should reduce the unit cost of COX-2 inhibitors

DoD faces difficulty in trying to address these two issues simultaneously. A closed class contract that offers BCF status for a COX-2 inhibitor could possibly achieve a significant price reduction, but many MTFs do not want COX-2 inhibitors to be added to the BCF. These MTFs do not have a COX-2 inhibitor on their formularies because they do not have sufficient funding and/or they want to target therapy by using the non-formulary special order process to provide COX-2 inhibitors only to patients who are at greatest risk for GI adverse events. The Council agreed that:

- The PEC should continue data analysis and provide feedback to MTFs to assist them in targeting therapy
- MTFs should analyze utilization and cost of COX-2s at the local level
- The PEC should obtain feedback from MTFs concerning methods they use to target COX-2 therapy and the accuracy and efficiency of those methods.
- A contract for COX-2 inhibitors should be pursued only if there is a mechanism to target therapy to patients who are at greatest risk for GI adverse events.

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

A. *Contract awards and renewals*

- The first joint DoD/VA closed class contract was awarded to Aventis Pharmaceuticals for the non-sedating antihistamine fexofenadine (Allegra) 60- and 180-mg tablets. The PEC previously issued implementation guidance for the non-sedating antihistamine contract (see Appendix B).
- DoD/VA single source contracts were awarded for the following drugs.
  - Ethinyl estradiol 35-mcg/norethindrone 1-mg tablets (Norinyl 1/35), 21s and 28s, to Watson Pharma
  - Norethindrone 35-mcg tablets (Nor-Q-D), 28s, to Watson Pharma
  - Ethinyl estradiol 35-mcg/1-mg ethynodiol diacetate (Demulen 1/35), 28s, to Pharmacia Corp.
  - Etodolac 200-, 300-mg capsules and 400-mg tablets, to Taro Pharmaceuticals
  - Hydrochlorothiazide 25-mg/50-mg tablets, to IVAX Pharmaceuticals (formerly Zenith-Goldline)
  - Prednisone 2.5-, 5-, 10-, 20-, and 50-mg tablets, to Pharmacia Corp.
  - Isosorbide mononitrate SA 30-, 60-, and 120-mg tablets, to Schwarz Pharma
  - Valproic Acid 250-mg capsules, to Sidmak Labs
  - Capsaicin 0.025% and 0.075% cream, to Qualitest Pharmaceuticals
  - Ticlopidine 250-mg tablets, to Par Pharmaceuticals
- As of 1 Jun 01, 44 joint VA/DoD national contracts have been awarded. Information on national pharmaceutical contracts, including NDC numbers and prices, is available on the DSCP website (www.dmmonline.com).

B. *Financial impact of contracts* – The estimated MTF cost avoidance due to national pharmaceutical contracts was $43.3 million for the first six months of FY 01. The $43.3 million in cost avoidance equals 7.9% of the $547.2 million that MTFs spent on pharmaceuticals through prime vendors during the first six months of FY 01. A summary of cost avoidance from national pharmaceutical contracts for FY 01 is provided in Appendix C.

C. *Report on Returned Goods Contract* – MAJ Cheryl Filby (DSCP) reported that, as of 5 June 01, 89 DoD facilities have signed up for the joint VA/DoD returned goods contract, which was awarded to Guaranteed Returns in Jan 01. More information on the Pharmaceutical Returns Management Program is available on the DSCP website at: http://dscp305.dscp.dla.mil/ dmmonline/pharm/return_program.asp

D. *Proton pump inhibitor contract* – Significant price reductions recently occurred in the proton pump inhibitor (PPI) market. Janssen lowered the FSS price of rabeprazole (Aciphex) to $0.22 per dose. In response to the market changes, the VA and TAP Pharmaceuticals have mutually agreed to cancel the VA's national contract for

lansoprazole (Prevacid) in favor of a BPA that sets the price for both strengths of lansoprazole at $0.55. Lansoprazole will remain on the VA National formulary, but the PPI class is now "open," so VA facilities may use other PPIs.

The DoD national contract price for omeprazole (Prilosec) is $1.09 per dose. The current option year expires on 30 Sep 01. The DoD P&T Executive Council strongly urges DSCP to negotiate a termination of the DoD national contract for omeprazole in a manner similar to what the VA negotiated.

E. *Potential contract for nasal corticosteroid inhalers* – The Council reiterated its support for establishing a joint VA/DoD closed class contract for a high potency aqueous nasal corticosteroid inhaler. Usage of nasal corticosteroid inhalers by pediatric patients should be taken into account in the contracting initiative.

F. *Potential contract for low molecular weight heparins/heparinoids (LMWHs)* — A closed class contract for a single LMWH for the outpatient treatment and prophylaxis of deep venous thrombosis (DVT) has been proposed. The Council assessed the therapeutic interchangeability of enoxaparin (Lovenox) and dalteparin (Fragmin) for outpatient treatment of DVT and prophylaxis of DVT and/or pulmonary embolism (PE) following hip or knee replacement surgery.

1) *Safety/Tolerability*

- Potential tolerability differences between the products are typically related to issues of administration (e.g., available syringe sizes) and are expected to be of relatively minor importance.
- The most important complication of anticoagulant therapy is bleeding. In a single head-to-head trial for prophylaxis of DVT following surgical repair of hip fracture, the incidence of major bleeding was 1/66 (1.5%) for dalteparin and 2/66 (3.0%) for enoxaparin. This was a small pilot study and may not represent the true incidence of major bleeding with either drug.
- Meta-analyses have found no significant difference between major bleeding rates with LMWHs and UFH, although differences have been reported in individual trials. In large clinical trials, major bleeding rates with UFH ranged from 0 to 7%, compared to 0 to 3% for LMWHs. It is difficult to draw any conclusion about the relative propensities of enoxaparin versus dalteparin to cause bleeding because of the lack of head-to-head data, differences in patient populations, dosing and regimen differences, and differences in how bleeding was defined across clinical trials.
- Enoxaparin and dalteparin are Pregnancy Category B and, unlike warfarin, are generally considered to be safe in pregnant patients requiring anticoagulation. According to case reports, patients with contraindications to warfarin have tolerated long-term use of dalteparin (2 months to 10 years) and enoxaparin (3 to 6 months).

2) *Efficacy for Outpatient Treatment of DVT*

- Enoxaparin is approved by the FDA for outpatient and inpatient treatment of DVT. Dalteparin is not approved by the FDA for treatment of either outpatient or inpatient treatment of DVT.
- There are no head-to-head trials comparing enoxaparin with dalteparin for treatment of DVT in either the inpatient or outpatient setting.
- *Enoxaparin vs. UFH* – Three large, well-conducted trials (two in the inpatient and one in the outpatient setting) compared enoxaparin with UFH for the treatment of DVT in a total of 917 patients. One trial also included patients with PE. No significant difference was noted in recurrent DVT/PE in the outpatient trial: enoxaparin 13/247 (5.3%); UFH, 17/254 (6.7%). However, only 33% of screened patients were considered eligible for study enrollment, and the studied population was generally at low risk for bleeding and did not have co-morbidities.
- *Dalteparin vs. UFH* – There are 11 published trials with dalteparin (seven in the inpatient and four in the outpatient setting) in a total of 1538 patients. However, while inpatient trials compared dalteparin with UFH, outpatient trials with dalteparin have not included an UFH comparison group. In a large (n=434), nonrandomized trial of dalteparin for the outpatient treatment of DVT, there were 7 cases of recurrent DVT (1.6%). These patients were considered to be at relatively low risk for bleeding and recurrent DVT/PE.
- Although most trials compared either dalteparin or enoxaparin to UFH, dalteparin trials were generally smaller and sometimes included patients with distal (calf vein) as well as proximal DVT (proximal DVT has a higher complication rate). Trials with enoxaparin primarily enrolled patients with proximal DVT. In addition, some of the dalteparin trials used surrogate efficacy measures (such as changes in thrombus size pre- and post-treatment) instead of clinical endpoints (such as incidence of recurrent DVT/PE). Comparison of the efficacy of the two drugs for outpatient treatment is further complicated by differences in patient populations (e.g., inclusion of patients with co-morbidities such as cancer, who are at increased risk for DVT/PE) resulting from differences in how patients were considered eligible for outpatient treatment.

3) *Efficacy for Prophylaxis of DVT Following Hip Replacement Surgery*

- Both enoxaparin and dalteparin are FDA-approved for DVT prophylaxis following hip replacement surgery.
- There are no head-to-head trials comparing enoxaparin with dalteparin in hip replacement surgery. Two trials compared dalteparin with warfarin and one trial compared enoxaparin with warfarin following hip replacement surgery. The incidence of symptomatic DVT/PE was lower with the LMWH than with warfarin in all three trials. There is insufficient evidence to conclude that enoxaparin and dalteparin differ significantly in efficacy for DVT prophylaxis following hip replacement surgery.

4) *Efficacy for Prophylaxis of DVT Following Knee Replacement Surgery*

- Of the two drugs, only enoxaparin is FDA-approved for DVT prophylaxis following knee replacement surgery.
- There are no head-to-head trials of enoxaparin and dalteparin for DVT prophylaxis. One double-blinded trial comparing enoxaparin and warfarin for DVT/PE prophylaxis following total knee replacement showed significantly fewer recurrent DVTs with enoxaparin compared to warfarin. There are no published trials that assess the efficacy of dalteparin for this indication.

5) *Other Factors*

- Enoxaparin is available as prefilled syringes in a wide range of dosages, which is an advantage for outpatient use. Dalteparin has only been available in pre-filled syringes in two dosages (2500- and 5000-U per 0.2 mL) and in a 10,000 U/mL multidose vial. Neither the prefilled syringes nor the multidose vial are optimal for the higher doses used for DVT treatment, which may require multiple injections. The manufacturer of dalteparin anticipates introduction of a higher concentration multidose vial and 7500- and 10,000-U prefilled syringes.
- Articles in the pharmacy literature report on at least two health systems that have changed from enoxaparin to dalteparin using a therapeutic interchange program. The program at one institution includes only DVT treatment and prophylaxis. Patients receiving enoxaparin for knee replacement surgery and cardiology indications are excluded. A preliminary drug usage evaluation comparing rates of recurrent DVT/PE and major bleeding between dalteparin and enoxaparin supported the feasibility of the therapeutic interchange program, but no outcome data are available. Another institution replaced enoxaparin with dalteparin in 1996 as the sole LMWH on the formulary for prophylaxis of DVT/PE following orthopedic and abdominal surgery. Rates of recurrent DVT/PE and major bleeding seen with dalteparin were comparable to those that would have been expected with enoxaparin.
- A total of 8298 LMWH prescriptions were filled at MTFs in FY 2000. Approximately 96% of these were for enoxaparin.
- *Input from MTF providers* – Because of the morbidity and mortality associated with DVT and PE, the PEC sent its clinical review of LMWHs and a survey requesting input regarding the therapeutic interchangeability of the LMWHs to 30 providers in Internal Medicine, Cardiology, Hematology/Oncology, Ob/Gyn, Emergency Medicine, Orthopedics, and Family Practice. A total of 12 surveys (40%) were returned. Three other physicians also provided comments. Survey results are summarized in the following table:

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
There are at least 2 LMWH products they would feel comfortable prescribing for DVT prevention/ treatment.	0	8	0	3	1
Providers would accept a contract for dalteparin for DVT prevention/treatment.	1	4	2	3	2
Providers would accept a contract for tinzaparin for DVT prevention/treatment.	0	4	1	5	2
Enoxaparin is used more because of familiarity than superiority.	1	4	0	5	0
Dalteparin is equal to enoxaparin for VTE treatment despite the lack of FDA approval.	0	6	0	3	2
Respondents would be more likely to be sued if a bad outcome occurred after prescribing dalteparin.	3	4	2	2	0

Given the morbidity and mortality associated with DVT/PE, the Council requires a high degree of certainty about the interchangeability of the drugs for these indications. The Council found insufficient data to confidently conclude that enoxaparin and dalteparin are equally efficacious for the outpatient treatment and prophylaxis of DVT. Although the survey of MTF providers revealed some support for a closed class contract, the responses showed insufficient support to pursue such a contract. The Council concluded that enoxaparin and dalteparin are not sufficiently interchangeable for a closed class contract for the outpatient treatment and prophylaxis of DVT.

G. *Role of the DoD P&T Executive Council in BPA development* –MAJ Cheryl Filby reported the recommendations of the subcommittee regarding the role of the DoD P&T Executive Council in the BPA development process. The Council voted to accept the subcommittee's recommendations:

- DSCP will coordinate all proposed DoD and DoD/VA blanket purchase agreements with the DoD P&T Executive Council (or the PEC acting on behalf of the Council) to ascertain whether the terms and conditions are in accord with the Council's strategy for managing the pertinent drug class. The DoD P&T Executive Council will accept or reject the terms of the agreement.
- If the P&T Executive Council accepts the agreement, DSCP will then be responsible for the content of the agreement in regard to legal and contractual sufficiency.
- Individual MTFs and TRICARE regions may continue to negotiate facility-specific incentive agreements. However, MTFs and TRICARE regions are encouraged to forward any agreements to DSCP for a review of legal sufficiency.

H. *Levofloxacin BPA* – At the Feb 01 meeting the Council asked DSCP to eliminate unacceptable provisions from the levofloxacin (Levaquin) BPA. The Council reviewed a revised BPA for levofloxacin and found that the unacceptable provisions had been eliminated. The BPA offers levofloxacin 250 mg and 500 mg to all MTFs for $2.00 per tablet. Continuation of the $2.00 price is contingent upon levofloxacin achieving either (1) an 80% aggregate DoD market share by 1 Aug 01, or (2) a 50% market share at individual MTFs. Market share will be based on patient days of therapy calculated from

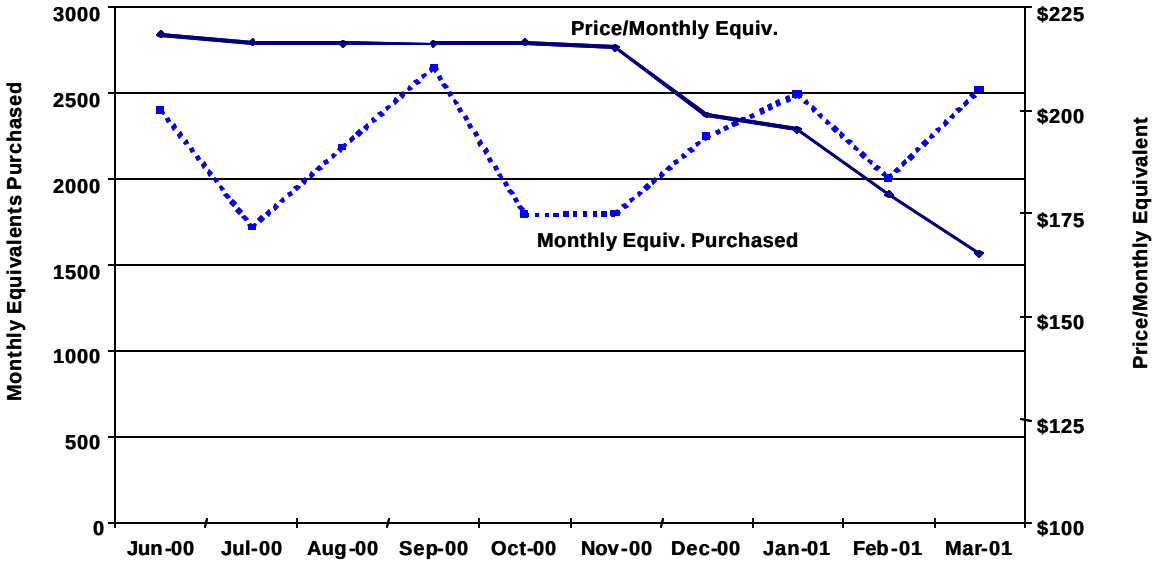
Uniformed Services Prescription Database (USPD) data. Levofloxacin is the only fluoroquinolone on the BCF, but the drug class remains "open," so MTFs may have additional fluoroquinolones on their formularies. As of April 2001, the aggregate market share for levofloxacin was approximately 77%.

I. *Status of BPAs for leutinizing hormone releasing hormone (LHRH) agonists* – A BPA makes goserelin (Zoladex) available to MTFs at the VA national contract price in exchange for attainment of an 80% overall share of the MTF prescriptions for LHRH agonists for prostate cancer by 1 Sep 2001.

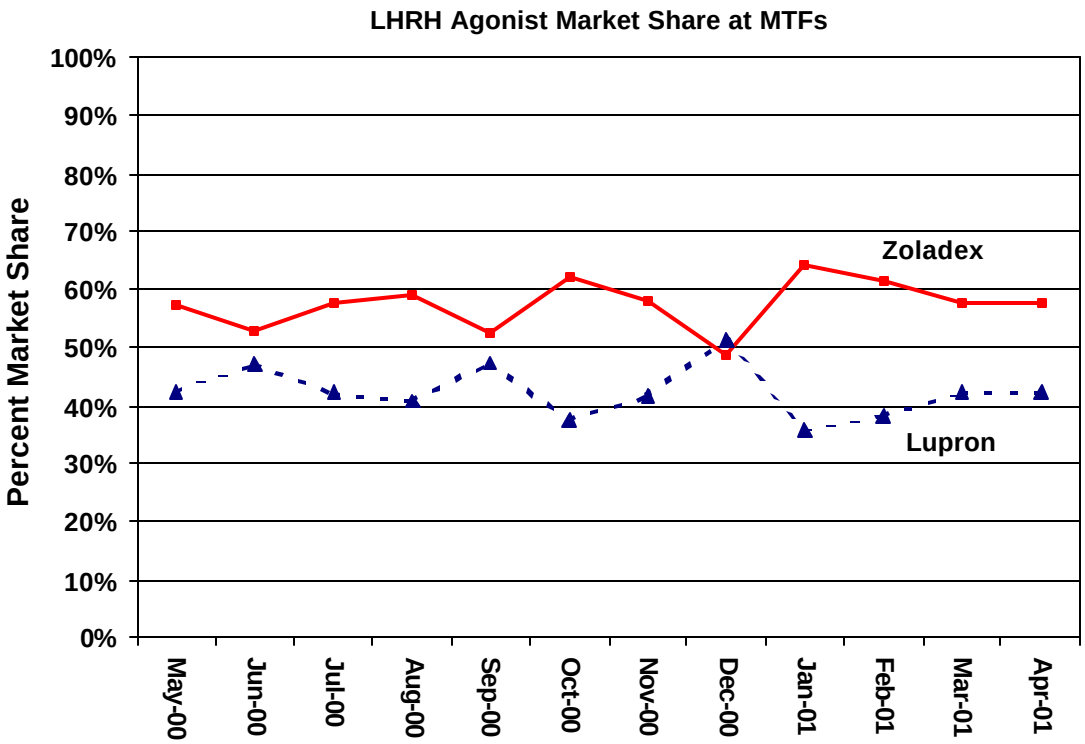
A BPA from TAP Pharmaceuticals makes leuprolide (Lupron) 1, 3, and 4-month depots available at a cost per dose just slightly higher than Zoladex. TAP modified the BPA in May 2001 so that the BPA price is available without any market share requirements (the original BPA required that Lupron attain an 80% market share within 6 months).

The Zoladex and Lupron BPAs have reduced the weighted average cost per monthly equivalent of LHRH agonist therapy for prostate cancer by 23% from $215 in Nov 00 to $165 in Mar 01. The BPAs yielded $294,000 in cost avoidance for MTFs from Nov 00 to Mar 01.

LHRH Agonist Price per Monthly Equivalent and Purchases at MTFs



Market share trends suggest that the 80% market share goal for Zoladex will probably not be achieved (see graph below). The Council asked DSCP and the PEC to talk with Astra Zeneca about the potential extension of the BPA price beyond August 2001 even if the 80% market share goal is not achieved.



The VA contract for Zoladex expires in February 2002. The Council asked the PEC to assess the potential for a contracting action for LHRH agonists for prostate cancer and present a recommendation at the August 2001 P&T Executive Council meeting.

J. *Proposed BPA for metformin/glyburide (Glucovance; BMS) and glyburide extended release (Glucophage XR; BMS)* – Bristol Myers Squibb (BMS) proposed a BPA that would reduce the price of Glucovance and Glucophage XR if they were added to the Basic Core Formulary. BMS also promised to further reduce the price of Glucovance and Glucophage XR to meet or beat any price offered on generic metformin until which point the generic metformin price falls below a price at which BMS can no longer compete. The proposed BPA did not specify the price at which BMS can no longer compete.

The Council concluded that there is insufficient evidence to prove conclusively that the extended release and combination dosage forms offer a clinically significant advantage regarding safety, tolerability, or efficacy over immediate release metformin or immediate release metformin plus generically available glyburide. While the proposed BPA would provide an economic benefit to DoD in the short run, it might be costly in the long run. DoD would benefit economically from the BPA until generic versions of metformin become available at a price below the BMS price protection point. If and when the price of generic metformin falls below the BMS price protection point, DoD would forgo the savings that could have been accrued through the use of the lower priced generic metformin because patients taking Glucovance or Glucophage XR would not likely switch back to generic metformin.

The current market share for various metformin products in MTF pharmacies, retail network pharmacies, and the NMOP are shown in the following table:

Number and percent of patient obtaining Rxs for various metformin products	MTFs	MCSC retail network	NMOP
Metformin (Glucophage)	42,756 (94%)	9,917 (72%)	4,912 (78%)
Extended release metformin (Glucophage XR)	2,401 (5%)	1872 (14%)	673 (11%)
Metformin/glyburide (Glucovance)	389 (1%)	1925 (14%)	722 (11%)
Totals	45,546	13,714	6,307

Note: time period is 4/1/01 through 5/25/01; data from the Pharmacy Data Transaction Service Customer Service Support Center

Since 94% of MTF patients using metformin products are currently using immediate release metformin (Glucophage), DoD has the potential to realize significant cost savings if these patients are treated with inexpensive generic versions of metformin in the future. The Council advised DSCP to reject the proposed BPA. The Council's rejection of the proposed BPA does not preclude an MTF from adding Glucovance or Glucophage XR to its formulary. MTFs should consider the local usage patterns and the degree to which their patients are getting prescriptions for Glucovance or Glucophage XR filled in retail pharmacies where the cost to DoD is much higher.

7. BCF ISSUES

A. *Proposal to add lancets to the BCF* – The Council decided not to add lancets to the BCF.

- Some MTFs provide lancets through central supply or other places in the MTF besides the pharmacy. There is no compelling reason to require all MTFs to provide lancets through the pharmacy.
- Standardization of medical and surgical supplies is being worked on a regional basis. Lancets and other items related to diabetic care might be more appropriately handled on a regional basis.

B. *Status of digoxin on the BCF* – The BCF listing for digoxin oral currently specifies Lanoxin brand (Glaxo Wellcome) only. The Council removed the specific brand designation from the listing because there is now an "A-rated" generic equivalent (Digitek; Bertek).

C. *Clarification of BCF listing for doxycycline oral* – Periostat (CollaGenex Pharmaceuticals) is a 20-mg capsule formulation of doxycycline hyclate with FDA approval as an adjunct to scaling and root planning to promote attachment level gain and pocket depth in patients with adult periodontitis. The mechanism of action is not antimicrobial, but is related to doxycycline's ability to inhibit collagenase.

The Council excluded Periostat from the BCF listing for doxycycline oral due to its low usage across the system (503 bottles of 100 purchased in the last 12 months, 65% of these by two large medical centers), its high cost relative to generic doxycycline, and the absence of a compelling reason to require all MTFs to have it on their formularies.

D. *Clarification of methylphenidate listing on the BCF* – The Council excluded Metadate CD from the BCF listing for methylphenidate oral.

- Metadate CD offers no safety or tolerability advantage compared to other dosage forms of methylphenidate already on the BCF.

- Metadate CD has an 8-hour duration of action. Concerta has a 12-hour duration of action and is on the BCF. With a shorter duration of action, Metadate CD is less likely than Concerta to eliminate the need for repetitive dosing.
- An FSS price is not yet available for Metadate CD and actual dose distributions for Metadate CD and Concerta are unknown, so a precise cost comparison is impossible. Assuming "standard" FSS pricing and a dosage distribution similar to that seen in clinical trials, the estimated weighted average daily cost of Metadate CD is $1.27. Concerta would be only slightly more expensive. The estimated weighted average daily cost for Concerta (based on manufacturer-supplied daily consumption data) is $1.42, $1.52 and $1.70 for the 54 mg, 36 mg and 18 mg strengths respectively.
- Metadate CD is a controlled substance, so all MTFs would experience the administrative burden associated with accounting for an additional controlled drug if Metadate CD were added to the BCF.
- The Council does not want to add another dosage form of methylphenidate to the BCF until it assesses how well Concerta reduces the frequency of midday dosing.

E. *Status of nifedipine extended release on the BCF* – The BCF listing for nifedipine extended release currently specifies Adalat CC as the BCF selection. At the last meeting, the DoD P&T committee requested that the PEC report back on whether the availability and pricing of generic nifedipine extended release products necessitated a change in the BCF listing. After reviewing the current availability and prices for generic versions of both Procardia XL and Adalat CC, the Council concluded that it is not necessary to make changes in the Basic Core Formulary until a generic manufacturer offers prices that are competitive with Adalat CC. The PEC will continue to monitor pricing for nifedipine extended release products.

8. MTF REQUESTS FOR BCF CHANGES

A. *Request to remove micronized glyburide from the BCF* – Glyburide oral and micronized glyburide are both listed on the BCF. An Air Force pharmacist requested that micronized glyburide be removed from the BCF because it is seldom used and more costly than other glyburide formulations. Alternately, he requested that a DoD or VA/DoD contracting initiative be considered to reduce the unit cost of the drug.

The safety, tolerability, and efficacy of glyburide and micronized glyburide appear to be similar. The primary difference between the formulations is improved and more consistent bioavailability with the micronized product, resulting in a less variable half-life and a lower propensity for food to interfere with absorption. The duration of action is similar with both drugs (16-24 hours), due to intracellular accumulation of glyburide. It is unclear whether the pharmacokinetic differences result in any improvement in glycemic control.

Generic micronized glyburide is at least 2 to 3 times more costly than generic glyburide. Of the 15.2 million sulfonylurea tablets or capsules purchased by MTFs through the Prime Vendor program during the first quarter of FY 01, 44% were glyburide; 43% glipizide, 10% micronized glyburide, 2% glimepiride, and essentially 0% tolazamide, tolbutamide, or chlorpropamide. A joint VA/DoD contracting initiative that includes micronized glyburide is already in progress.

The Council did not make any changes to the BCF pending results of the contracting initiative for micronized glyburide.

B. *Request to add gatifloxacin (Tequin) and remove levofloxacin (Levaquin) from the BCF* – A Director of Pharmacy Services at an Air Force MTF cited a price advantage for gatifloxacin in a request to replace levofloxacin with gatifloxacin on the BCF. Gatifloxacin is available to MTFs through an incentive price agreement at a price of $1.90 for the 200 mg and 400 mg tablets. The incentive price is contingent on gatifloxacin having a preferred or co-preferred formulary position at an individual MTF, but there are no market share requirements.

   The Council voted to keep levofloxacin on the BCF. Removal of levofloxacin from the BCF would nullify the BPA that makes levofloxacin available to all MTFs at a price of $2.00 per dose. MTFs are reminded that the fluoroquinolone class is open on the BCF, so MTFs may add gatifloxacin to their formularies if they wish to take advantage of the lower price for gatifloxacin.

C. *Requests to add tolterodine extended release capsules (Detrol LA) to the BCF* – MAJ Roach reported that the PEC received 10 requests for addition of Detrol LA to the BCF in a single week. With the exception of one request from an obstetrician-gynecologist, the requests came from specialty providers (urogynecology or urology). Four requestors noted that tolterodine extended release should be considered a second line agent after the patient has failed oxybutynin; two of the four specifically mentioned tolerability and compliance benefits in elderly patients who could not tolerate oxybutynin. Three requestors cited comparable costs for the tolterodine immediate release and extended release preparations. One requestor felt that tolterodine had become standard of care in community and academic practice for treatment of Overactive Bladder (OAB). The Council considered these requests as part of the overall review of OAB drugs (see Paragraph 9C).

D. *Review of form for requesting BCF changes on PEC website* – MAJ Roach reported that requestors provided little information about how the requested drug compared to other drugs regarding safety, tolerability, efficacy and price. The Council agreed with the PEC recommendation to change the wording on the form to more clearly ask MTF providers to compare the requested agents to other drugs on the BCF or in the same drug class.

9. BASIC CORE FORMULARY REVIEW

A. *Ongoing review* – The PEC is reviewing topical medications for acne and benzodiazepines for anxiety disorders. Information on these drugs will be presented at the next meeting of the P&T Executive Council.

B. *Review of topical corticosteroids for the BCF* – MAJ Barbara Roach reported on the PEC review of topical corticosteroids (see Appendix D for a table of topical corticosteroid agents). Topical corticosteroids were grouped by potency category, ranging from Class I (Very High Potency Agents) to Class IV (Low Potency Agents). According to input from dermatologists, primary care providers, and others, there is little or no difference within potency categories except for the difference between fluorinated and nonfluorinated agents and availability in the desired vehicle (e.g., ointment, cream). The Council considered each potency category for potential changes to the BCF:

Class I Agents (Very High Potency) – There is currently no Class I agent on the BCF. These agents are not generally considered to be primary care drugs. No agent from this class was added to the BCF.

Class II Agents (High Potency) – There are currently no Class II agents on the BCF. After considering the opinions of dermatologists and primary care providers and the relative usage and cost per gram for specific agents within this category, the Council decided to add fluocinonide 0.05% cream to the BCF.

Fluocinonide represents 58% of all MTF purchases of Class II agents (by number of tubes) and is available under a VA/DoD national contract at approximately $0.10 per gram. (Costs per gram in this category range as high as $1.17 per gram). Fluocinonide 0.05% cream represents the great majority of all purchases of fluocinonide products. MTFs may decide whether or not to add fluocinonide 0.05% ointment or solution to their formularies according to local usage patterns.

Class III Agents (Medium Potency) – Triamcinolone 0.1% is currently listed on the BCF as "triamcinolone acetonide 0.1% topical." The Council did not add another Class III agent to the BCF.

The Council agreed that listings for topical agents on the BCF should specify formulation (e.g., cream, ointment) and concentration. After considering the relative usage of the various formulations, the Council clarified the listing to "triamcinolone acetonide 0.1% cream." To avoid confusion, the Council instructed the PEC to clarify the definitions section on the BCF page of the PEC website to note that formulary requirements for topical agents include only the specified formulation(s) and strength(s). The PEC will review the BCF to see if further clarifications are necessary for individual topical agents.

Class IV Agents (Low Potency) – The only low potency topical corticosteroid on the BCF is hydrocortisone 2.5% rectal cream. The Council discussed addition of a Class IV nonfluorinated topical corticosteroid agent for general use. Nonfluorinated agents cause less skin atrophy than fluorinated agents, which is particularly important for pediatric patients and for administration to the face.

The majority of MTFs already have hydrocortisone cream on their individual formularies and many also have desonide (both are nonfluorinated). Hydrocortisone cream and ointment are available in both OTC and prescription formulations. The BCF generally does not include OTC medications, so the Council did not add hydrocortisone cream or ointment to the BCF. The Council also did not add desonide to the BCF because it costs approximately eight times more per gram than hydrocortisone, and the Council did not wish to mandate that facilities using hydrocortisone cream must also add desonide to their formularies.

C. *Review of medications for overactive bladder (OAB) for the BCF* – Oxybutynin immediate release is the only medication for overactive bladder currently on the BCF. Tolterodine (Detrol, Detrol LA) and oxybutynin extended release (Ditropan XL) have a lower incidence of anticholinergic side effects (e.g. dry mouth) than oxybutynin immediate release. The clinical significance of the lower incidence of side effects is uncertain because the percentage of patients who discontinued these drugs due to side effects in clinical trials is small and not clinically or statistically different between the

drugs. Ditropan XL, Detrol, and Detrol LA all cost more than 10 times as much as oxybutynin immediate release. The Council concluded that Ditropan XL, Detrol, and Detrol LA should not be added to the BCF because they do not offer sufficient clinical benefit to justify their significantly higher cost compared to oxybutynin immediate release.

D. *Review of sedative/hypnotic medications for the BCF* – Temazepam and zolpidem currently account for over 90% of sedative/hypnotic medications dispensed from MTF pharmacies. One or more of these drugs are present on 90% of MTF formularies, and 55% of MTFs have both drugs on formulary. The Council considered only these two sedative/hypnotic medications for addition to the BCF.

   Eighty percent of MTFs have temazepam on formulary, but prime vendor data show that usage is declining. Council members speculated that usage is shifting toward newer agents that might have a lower propensity to cause tolerance and dependence in long term use). The Council concluded that temazepam should not be added to the BCF because there is no clinical reason to require 20% of the MTFs to add it to their formularies.

   Sixty-five percent of MTFs have zolpidem on formulary. Anecdotal reports suggest continued efficacy of zolpidem in long-term use without the development of tolerance or dependence; however, clinical trial evidence is limited to trials of 35 days or less. Zolpidem costs more than 40 times as much as temazepam. The Council concluded that zolpidem should not be added to the BCF because the magnitude of the incremental clinical benefit is uncertain and the incremental cost is too large to require every MTF to have it on their formularies.

   No changes were made to the BCF. The sedative/hypnotic class will not be represented on the BCF at this time.

10. The meeting adjourned at 0900 hours on 7 June 2001. The next meeting will be held at Ft Sam Houston, TX and is scheduled for 15 Aug 01 at 0800. All agenda items should be submitted to the co-chairs no later than 20 Jul 01.

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

LIST OF APPENDICES

Appendix A: MTF Expenditures for Drugs Included in the Advances in Medical Practice (AMP) Program

MTF Expenditures on AMP Drugs, First Six Months of FY 01

Drug Name*	Air Force	Army	Navy	Grand Total
Abciximab	$153,356	$135,960	$61,384	$350,699
Alpha-1-Proteinase Inhibitor			$5,676	$5,676
Becaplermin	$42,589	$55,966	$28,194	$126,749
Cyclosporine	$229,898	$157,445	$119,904	$507,247
Cyclosporine Microemulsion	$465,749	$425,208	$436,010	$1,326,967
Dornase Alfa	$160,855	$92,255	$112,092	$365,203
Epoetin Alfa	$2,083,361	$2,444,833	$1,197,215	$5,725,408
Eptifibatide	$38,665	$198,383	$124,977	$362,025
Etanercept	$804,539	$529,045	$300,484	$1,634,069
Factor VIIa,Recomb				
Filgrastim	$713,677	$880,520	$499,944	$2,094,141
Gemcitabine Hcl	$107,075	$205,731	$123,202	$436,008
Glatiramer Acetate	$258,059	$116,704	$64,836	$439,600
Infliximab	$153,880	$153,784	$187,743	$495,407
Interferon Beta-1a	$851,257	$632,273	$322,213	$1,805,742
Interferon Beta-1b	$280,715	$361,135	$237,275	$879,125
Interferon Gamma-1b,Recomb.	$30,794	$25,793	$20,854	$77,441
Irinotecan Hcl	$114,396	$303,743	$126,862	$545,001
Leflunomide	$105,700	$189,325	$103,047	$398,072
Mycophenolate Mofetil	$282,012	$333,083	$151,995	$767,090
Mycophenolate Mofetil HCl	$460	$1,681		$2,141
Palivizumab	$1,261,189	$1,294,001	$851,639	$3,406,830
Ribavirin/Interferon A-2b	$398,410	$899,484	$297,228	$1,595,122
Rituximab	$143,969	$660,609	$203,242	$1,007,820
Sargramostim	$14,918	$75,739	$7,850	$98,507
Sirolimus	$20,452	$43,216	$22,488	$86,155
Tacrolimus Anhydrous	$293,731	$241,897	$167,910	$703,538
Temozolomide	$83,072	$72,879	$51,571	$207,522
Tirofib Hc M-Hyd/Na Chlor 0.9%	$2,023	$21,087		$23,109
Tirofiban HCl M-Hydrate	$62,628	$47,964	$15,166	$125,759
Trastuzumab	$69,227	$153,578	$10,647	$233,452
Grand Total	**$9,226,657**	**$10,753,321**	**$5,851,648**	**$25,831,626**

* Celecoxib and rofecoxib were removed from the AMP list for FY 01

Appendix B: Implementation Guidance for the Non-Sedating Antihistamine Contract

Note: The following implementation plan was distributed to the field via e-mail the last week of April 2001.

Implementation Plan for the Non-Sedating Antihistamine Contract

Department of Defense Pharmacoeconomic Center

Effective Date: 1 May 2001 (Contract will be in effect for one year with an option to extend the terms of the contract for 4 additional one-year periods).

Selected Product: Fexofenadine (Allegra®) 60 mg tablets and 180 mg tablets; Aventis Pharmaceuticals Inc.

Contract Prices

Table 1

Strength	Dosage Form	NDC	Price per tablet/capsule	QTY per Package
60 mg	Tablet	00088-1107-47	$0.37	100
60 mg	Capsule*	00088-1102-55	$0.37	500
180 mg	Tablet	00088-1109-47	$0.60	100

* Aventis Pharmaceuticals informed the Pharmacoeconomic Center that production of the Allegra® 60mg capsule product will be phased out over the next 12 months. The contract price of $0.37 for the 60mg capsule only applies to the 500-count package size. The contract price for the 60mg capsule will only apply until such time that the 500-count package size of the Allegra 60mg tablet is available. We suggest that MTFs **not** add the 60 mg capsule to their formularies, as it will necessitate switching patients to the tablet formulation in the near future.

Formulary guidance

- This contract closes the non-sedating antihistamine (NSA) class on the Basic Core Formulary (BCF) and therefore:
  1) Allegra® 60 mg tablets and Allegra® 180 mg tablets must be on all Military Treatment Facility (MTF) formularies.
  2) Claritin® 10 mg tablets and Claritin Reditabs® must not be on any MTF formularies.
- Table 2 delineates formulary status requirements for all Allegra® and Claritin® products. While MTFs are not precluded from having the products in column 3 on formulary, MTFs should only include these products on formulary if the needs of their specific patient population require their availability. This decision requires critical evaluation of the relative costs of all products that can meet the clinical needs of patients.

Table 2

MTFs must have on formulary:	MTFs cannot have on formulary:	MTFs may have on formulary:
Allegra 180 mg tablets	Claritin Reditabs	Allegra 60 mg capsules
Allegra 60 mg tablets	Claritin 10 mg tablets	Allegra 30 mg tablets
		Allegra D
		Claritin Syrup
		Claritin D 12 Hour
		Claritin D 24 Hour

- Other NSAs that may be approved by the FDA after the date of this announcement may not be added to MTF formularies during the term of this contract.
- Cetirizine (Zyrtec®) is classified as a second-generation antihistamine but is not classified as an NSA. Therefore, this contract does not affect the current or future BCF or MTF formulary status of Zyrtec® products.
- This contract does **not** affect the current or future status of any Allegra®, Claritin®, or Zyrtec® product on the National Mail Order Pharmacy (NMOP) formulary. All Allegra®, Claritin® and Zyrtec® products remain available through the NMOP. Please note that the contract price for the Allegra® products as presented in Table 1 *will* apply to the NMOP.
- This contract does **not** apply to Managed Care Support Contractor retail network pharmacies.

Prescribing guidance for prescriptions filled at MTFs

- **New patient starts (patients who have not previously been prescribed a Claritin â or Allegra â product):** The contract requires that all new patients who have a clinical need for an NSA be prescribed either Allegra® 60 mg tablets or Allegra®180 mg tablets. If the patient fails to achieve adequate symptom relief or experiences unacceptable side effects with Allegra®, it is permissible to prescribe Claritin® under the provisions of medical necessity. Other examples of medical necessity include:
  - documented allergy to Allegra® products
  - pregnant patients with a clinical need for an NSA (Claritin® is assigned a pregnancy risk category B. Allegra® is assigned a pregnancy risk category C)
- **Patient who were previously treated successfully with Claritin 10mg or Claritin Reditabs:** Unlike the contracts currently in place for the proton pump inhibitor and statin drug classes, this contract does not mandate the conversion of NSA patients currently receiving Claritin® 10 mg tablets or Claritin Reditabs® to Allegra® 60 mg tablets or Allegra® 180 mg tablets. It is therefore **permissible** for patients who were successfully treated with Claritin® 10 mg tablets or Claritin Reditabs® to continue to receive these products. However, it is important to note that while the contract does not mandate patients be switched, **MTFs may decide to encourage their providers to switch patients.** This decision will be made at the MTF level.
- This contract does not preclude providers from prescribing alternate agents to patients for whom the contracted dosage forms and strengths are clinically inappropriate (i.e., pediatric patients).
- Both Allegra® 180 mg tablets and Allegra® 60 mg tablets are included in the NSA contract. This gives providers greater flexibility by allowing them to prescribe either Allegra® 60 mg in the morning and a generic sedating antihistamine in the evening at a cost of approximately $0.40 per day, Allegra® 180 mg once daily at a cost of $0.60 per day, or Allegra® 60 mg twice daily at a cost of $0.74 per day.

Points of Contact:

Note: Points of contact changed from initial version due to personnel changes at the Pharmacoeconomic Center

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Appendix C: Cost Avoidance in DoD MTFs Due to National Pharmaceutical Contracts, First 6 months of FY01 (Oct 00 – Mar 01)

Estimated Cost Avoidance in DoD MTFs Due to National Pharmaceutical Contracts, First Six Months of Fiscal Year 2001						
Drug/Drug Class	**Contract Start Date**	**Weighted Average Price/Unit Before Contract**	**Theoretical 1st and 2nd Quarter FY 01 Cost If Not Contracted**	**1st and 2nd Quarter FY 01 Actual Cost**	**Cost Avoidance**	**Percent Reduction in Cost**
Statins	1-Oct-99	$0.961874	$40,684,953	$31,484,021	$14,510,274	35.66%
PPIs	1-Oct-99	$1.681407	$50,953,184	$34,252,261	$16,700,923	32.78%
Lisinopril	1-Aug-99	$0.284396	$11,378,013	$6,869,586	$4,508,426	39.62%
Diltiazem	15-Dec-98	$0.631469	$6,373,438	$3,493,867	$2,879,571	45.18%
Ranitidine	16-Nov-98	$0.066602	$1,841,140	$1,544,368	$296,772	16.12%
Hepatitis A	18-Sep-99	$16.981597	$4,452,914	$2,967,127	$1,485,788	33.37%
Albuterol	16-Nov-98	$3.297032	$1,437,275	$1,749,002	($311,727)	-21.69%
Timolol Gel	14-Jan-00	$14.598153	$625,487	$255,067	$370,420	59.22%
Verapamil	20-Aug-99	$0.125912	$1,188,225	$821,203	$367,022	30.89%
Cimetidine	16-Nov-98	$0.072763	$332,088	$187,941	$144,147	43.41%
Terazosin	5-Sep-00	$0.459093	$4,014,631	$1,991,315	$2,023,316	50.40%
Captopril	18-Oct-99	$0.036173	$97,191	$56,579	$40,612	41.79%
Nortriptyline	15-Oct-99	$0.049281	$151,200	$111,120	$40,079	26.51%
Gemfibrozil	1-Jan-00	$0.077935	$530,685	$536,119	($5,433)	-1.02%
Naproxen	3-Jul-00	$0.069829	$1,384,510	$1,363,885	$20,625	1.49%
Amoxicillin	7-Aug-99	$0.040549	$291,247	$286,829	$4,417	1.52%
Insulin Syringes	1-May-00	$0.098121	$577,609	$407,346	$170,263	29.48%
Timolol Drops	14-Jan-00	$2.795264	$115,908	$94,615	$21,294	18.37%
Nicotine Patches	1-Jun-00	$2.567746	$751,541	$638,886	$112,654	14.99%
Levobunolol	14-Jan-00	$4.641527	$30,356	$21,778	$8,578	28.26%
Fluocinonide	1-Sep-99	Cream $1.816402 Oint $6.210282 Sol $6.422653	$179,959	$178,805	$1,154	0.64%
Prazosin	1-Nov-99	$0.032916	$63,057	$55,562	$7,495	11.89%
Amantadine	28-Aug-99	$0.063871	$31,744	$28,649	$3,095	9.75%
Naproxen Sodium	3-Jul-00	$0.073176	$78,586	$74,645	$3,941	5.01%
Salsalate	15-Mar-00	$0.026462	$59,335	$74,599	($15,264)	-25.73%
Insulin	1-Nov-99	$5.292812	$2,593,605	$2,726,349	($132,744)	-5.12%
Acyclovir	1-Oct-00	$0.121623	$462,557	$414,140	$48,416	10.47%
Azathioprine	1-Oct-00	$0.477152	$389,785	$349,282	$40,503	10.39%
Hydroxyurea	1-Oct-00	$0.295324	$78,497	$79,258	($761)	-0.97%
Pentoxifylline	1-Oct-00	$0.182262	$385,192	$383,409	$1,782	0.46%
Rifampin	1-Oct-00	$0.566776	$93,201	$86,415	$6,786	7.28%
Sucralfate	1-Oct-00	$0.198476	$192,692	$192,541	$152	0.08%
Acetaminophen	1-Jan-01		NA	NA	NA	NA
TOTAL			**$131,819,804**	**$93,776,570**	**$43,352,575**	**32.89%**

Explanation of Cost Avoidance Calculations: Cost avoidance equals the difference between (1) the theoretical cost that would have occurred in FY 00 if a contract had not existed, and (2) the actual cost that was incurred in FY 01 for the "market basket" of drugs that pertains to each contract. The theoretical cost that would have occurred in FY 01 if a contract had not existed was estimated by multiplying the weighted average price/unit that existed before the contract took effect by the quantity purchased in FY 01. The "market basket" of drugs includes both the contracted and the non-contracted drugs that pertain to a given contract. For example, the cost avoidance for statins takes into account the expenditures for all six statins, not just the two contracted statins.

Appendix D –Topical Corticosteroid Table

After receiving input from dermatology consultants, providers, and pharmacists, topical corticosteroids were divided into four categories depending on potency. The potency of a topical corticosteroid is standardized according to its ability to induce vasoconstriction. This is partially determined by the concentration of the drug and the vehicle used. The categories range from Class I (Very High Potency Agents) to Class IV (Low Potency Agents).

Ranking the topical corticosteroids in this manner may present some discordance among different classification schemes when attempting to categorize a specific drug into a particular level of potency; overall, however, disagreements are minor. Disease severity, age, body location and concomitant medical conditions usually determine the potency of topical corticosteroid treatment, while characteristics of the dermatologic condition usually determine the vehicle chosen. There appears to be little clinical reason to prefer one drug to another within a given category except for availability in the desired vehicle and a preference for nonfluorinated products for pediatric use or use on the face. Nonfluorinated products appear to cause less skin thinning (atrophy).

Topical Corticosteroids Categorized by Potency

Class I – Very High Potency			
Brand Name	**Generic Name**	**Vehicle**	**(%)***
Diprolene	Augmented betamethasone dipropionate	Ointment	0.05
Temovate, Cormax, Temovate E	Clobetasol propionate	Cream, Ointment, Gel, Solution	0.05
Psorcon	Diflorasone diacetate	Ointment	0.05
Ultravate	Halobetasol propionate	Cream, Ointment	0.05

Class II – High potency			
Brand Name	**Generic Name**	**Vehicle**	**(%)***
Cyclocort	Amcinonide	Cream, Ointment, Lotion	0.1
Diprolene AF	Augmented betamethasone dipropionate	Cream	0.05
Alphatrex, Del-Beta, Diprosone, Maxivate	Betamethasone dipropionate	Cream, Ointment, Lotion	0.05
Betatrex	Betamethasone valerate	Ointment	0.1
Topicort	Desoximetasone	Cream, Ointment Gel	0.25 0.05
Florone, Florene-E emollient, Maxiflor	Diflorasone diacetate	Cream, Ointment (emollient base)	0.05
Synalar-HP	Fluocinolone acetonide	Cream	0.2
Lidex, Lidex-E, Lidex soln.	Fluocinonide	Cream, Ointment, Solution, Gel	0.05
Halog (water soln cream), Halog solution, Halog-E	Halcinonide	Cream, Ointment, Solution	0.1
Aristocort, Aristocort A Kenalog, Trymex	Triamcinolone acetonide	Cream, Ointment	0.5

Topical Corticosteroids Categorized by Potency (continued)

Class III – Medium potency			
Brand Name	**Generic Name**	**Vehicle**	**(%)***
Benisone, Uticort	Betamethasone benzoate	Cream, Gel, Lotion	0.025
Alphatrex, Diprosone	Betamethasone dipropionate	Lotion	0.05
Valisone, Beta-Val, Betatrex	Betamethasone valerate	Cream, Lotion	0.1
Cloderm	Clocortolone pivalate	Cream	0.1
Topicort LP	Desoximetasone	Cream, Gel	0.05
Fluonide, Synalar, Synemol	Fluocinolone acetonide	Cream, Ointment	0.025
Cordran	Fluandrenolide	Cream, Ointment Lotion	0.025, 0.05 0.05
Cutivate	Fluticasone propionate	Cream Ointment	0.05 0.005
Locoid	Hydrocortisone butyrate	Cream, Ointment, Solution	0.1
Westcort	Hydrocortisone valerate	Cream, Ointment	0.2
Elocon	Mometasone furoate	Cream, Ointment Lotion	0.1
Aristocort A, Kenalog, Trymex,	Triamcinolone acetonide	Cream, Ointment Lotion	0.025 0.025, 0.1

Class IV – Low potency			
Brand Name	**Generic Name**	**Vehicle**	**(%)***
Aclovate	Alclometasone dipropionate	Cream, Ointment	0.05
Valisone, Celestone	Betamethasone valerate	Cream	0.01, 0.2
DesOwen, Tridesilon	Desonide	Cream, Ointment, Lotion	0.05
Decaderm	Dexamethasone	Gel	0.1
Synalar, Fluonid	Fluocinolone acetonide	Cream, Solution	0.01
Hytone, Lacticare, Synacort	Hydrocortisone	Lotion Cream, Oint, Lotion Cream, Oint, Lotion, Solution Cream, Oint, Lotion	0.25 0.5 1 2.5
Numerous	Hydrocortisone acetate	Cream, Ointment	0.5, 1
Medrol	Methylprednisolone	Cream	0.25
Oxylone	Fluoromethalone	Cream	0.025
Numerous OTCs			

fluorinated agent; nonfluorinated agent; disagreement among references concerning potency class

* Not all brands or concentrations are available in all vehicles or formulations; specialized formulations such as aerosols or tapes are not included in this table

Department of Defense
Pharmacoeconomic Center

1750 Greeley Rd., Bldg. 4011, Rm. 217
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MCCS-GPE **8 FEB 2001**

MEMORANDUM FOR: Executive Director of 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 February 2001, at Ft Sam Houston, TX.

2. **MEMBERS PRESENT**:

CDR Terrance Egland, MC	Co-chair
COL Daniel D. Remund, MS	Co-chair
COL Mark Nadeau, MC	Air Force (alternate)
COL (select) John R. Downs, MC	Air Force
MAJ George Jones, BSC	Air Force
CDR Matt Nutaitis, MC	Navy
MAJ Brett Kelly, MS	Army
CDR Robert Rist	Coast Guard
Ronald L. Mosier	Department of Veterans Affairs
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia (DSCP)
Trevor Rabie	Uniformed Services Family Health Plans (USFHP)
Ray Nan Berry	Health Net Federal Services
Kirby Davis	Anthem Alliance
William Hudson	Humana, Inc
Gene Lakey	TriWest

MEMBERS ABSENT:

COL Rosa Stith, MC	Army
LTC Judith O'Connor, MC	Army
CDR Kevin Cook, MSC	Navy
Ron McDonald	Sierra Military Health Services
Joint Readiness Clinical Advisory Board Representative	

OTHERS PRESENT:

CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
COL Mike Heath, MS	Army Pharmacy Consultant, DoD Pharmacy Board of Directors
CDR Mark Brouker, MSC	DoD Pharmacoeconomic Center
COL William Davies, MS	DoD Pharmacy Program Director, Tricare Management Activity (TMA)
LTC Don De Groff, MS	DoD Pharmacoeconomic Center
LTC Ed Zastawny, BSC	DoD Pharmacoeconomic Center
LCDR Ted Briski, MSC	Lead Agent Office, Region 9
MAJ Cheryl Filby, MS	Defense Supply Center Philadelphia
CAPT Krissa Crawford, BSC	Pharmacy Practice Resident, Wilford Hall Medical Center
HM3 Cory Beckner	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
David Chicoine	Uniformed Services Family Health Plan
Eugene Moore	DoD Pharmacoeconomic Center
Mark Petruzzi	Merck-Medco
Elizabeth Scaturro	Merck-Medco
Carol Scott	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
Dana Dallas	Defense Supply Center Philadelphia
Paul Vasquez	Defense Supply Center Philadelphia

3. **ADMINISTRATIVE ISSUES**

   The minutes from the last meeting were accepted as written.

4. **REPORT FROM THE DOD EXECUTIVE COUNCIL MEETING** – COL Remund reported that the DoD P&T Executive Council added 12 drugs to the Basic Core Formulary (BCF) at the 7 Feb 01 meeting. Budget shortfalls in the Defense Health Program for FY 01 forced the Council to be very conservative in adding drugs to the BCF.

5. **IMPLEMENTATION OF FY 00 AND FY 01 NATIONAL DEFENSE AUTHORIZATION ACTS** – COL Davies briefed the Committee on the ongoing efforts to implement the pharmacy benefit provisions of the FY 00 and FY 01 National Defense Authorization Acts.

6. **BCF AND NATIONAL MAIL ORDER PHARMACY (NMOP) FORMULARY ISSUES** – The Committee determined the NMOP formulary status; NMOP or retail network formulary restrictions (NMOP Preferred Drug Program, quantity limits, or prior authorization); and the BCF status for six new drugs listed in Appendix A.

7. **NON-PREFERRED/PREFERRED DRUG PAIRS IN THE NMOP** – Eugene Moore (PEC) reported cost avoidance associated with the NMOP Preferred Drug Program (see Appendix B).

8. PRIOR AUTHORIZATIONS

A. *Cost avoidance from NMOP prior authorizations (PAs)* – Shana Trice (PEC) reported on the estimated cost avoidance due to NMOP prior authorizations. The cost avoidance per prescription is based on the cost avoidance model that was outlined in the Aug 00 DoD P&T Committee minutes.

PA Cost Avoidance per New Prescription Submitted to the NMOP

Drug	3rd Quarter FY 00	4th Quarter FY 00	1st Quarter FY 01
Sildenafil	$13.60	$26.46	Not calculated
COX-2 inhibitors	$11.66	$18.56	$10.95
Etanercept	$327.20	$111.86	$7.89

1) *Sildenafil* – Data reported by Merck Medco and DSCP suggest that a large number of the PAs performed during the first quarter FY 01 were for sildenafil refills. PA cost avoidance was not calculated for the first quarter of FY 01 because the cost avoidance model was not designed to account for prior authorization of refill prescriptions. The PEC will work with Merck Medco and DSCP to revise the model.

2) *Etanercept* – The large drop in the PA cost avoidance for etanercept is due to fewer prescription denials through the PA process (see following table).

NMOP PA Data for Etanercept

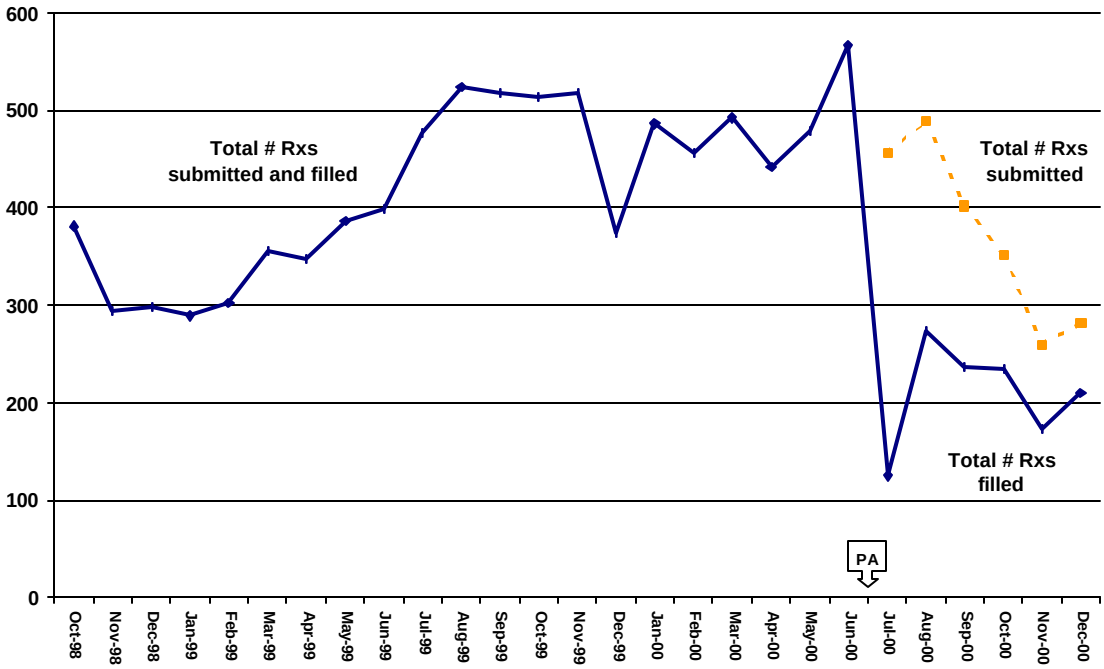
	3rd Quarter FY 00	4th Quarter FY 00	1st Quarter FY 01
Total number of Rxs filled (new and refill)	441	495	612
Total number of Rxs that went through the PA process	41	64	58
Total number of Rxs denied as a result of the PA process	11	5	1
Estimated cost avoidance per new Rx submitted	$327.20	$111.86	$7.89

The Committee discussed the possibility of modifying or discontinuing the PA for etanercept since the cost avoidance is so minimal. The Committee refrained from changing the etanercept PA because this analysis does not assess the PA cost avoidance in the retail pharmacy networks (which probably fill many more prescriptions for etanercept than the NMOP). The Committee encouraged the MCSC pharmacy directors to voluntarily provide data to the PEC for analysis of the etanercept PA cost avoidance in the retail networks (the MCSC pharmacy directors are not contractually required to submit the data). The PEC will furnish a list of data elements in the cost avoidance model to the MCSC pharmacy directors.

B. *Antifungals for onychomycosis* – The PA for onychomycosis began on 1 Jul 00 in the NMOP. Comparing the six-month time periods before and after the PA took effect, prescription fills for terbinafine and itraconazole dropped from an average of 491 per month (range 444-569) to an average of 211 per month (range 129-239). Prescription fills for terbinafine and itraconazole dropped because (1) prescriptions submitted to the NMOP were denied when they did not meet

the PA criteria, and (2) fewer prescriptions for terbinafine and itraconazole were submitted to the NMOP due to the "sentinel" effect of the PA. The sentinel effect occurs because providers prescribe the drug less frequently when they know the drug is subject to prior authorization. The following graph illustrates the reduction in the number of prescriptions submitted and the number of prescriptions filled for terbinafine and itraconazole after the PA began.

Total Number of NMOP Rxs for Terbinafine or Itraconazole



C. *Revision of PA forms* – Merck-Medco added clinical rationale language to the PA forms it faxes to prescribers for sildenafil and etanercept. The clinical rationale language is not yet in place on the Merck-Medco PA fax forms for COX-2 inhibitors or antifungals for onychomycosis.

D. *Changes to COX-2 inhibitor criteria to include Familial Adenomatous Polyposis (FAP)* – At the Aug 00 meeting, the Committee approved a change in the criteria for the COX-2 inhibitors to allow use of celecoxib for familial adenomatous polyposis. Merck-Medco has revised their fax form. The PEC will reflect the changes on its website.

E. *Proposal to change the COX-2 inhibitor PA to reflect findings of the Celecoxib Long-term Arthritis Safety Study (CLASS)* – The annualized incidence rates of upper GI ulcer complications alone and combined with symptomatic ulcers were not significantly different for celecoxib versus NSAIDS for patients in the CLASS study who were also receiving low dose aspirin. The data, however, were limited: the number of patient-years of therapy for patients also receiving low dose aspirin was relatively low, results were based on a maximum of 6 months of therapy, and the dropout rates in both the celecoxib and NSAID group were high (40-45%).

The CLASS study suggests that the use of even low doses of aspirin may reduce or eliminate the GI protective effect of COX-2 selective NSAIDs compared to conventional NSAIDS. However, the Committee agreed that the data are insufficient to change the PA criteria to preclude usage of COX-2 inhibitors by patients taking low dose aspirin. The Committee requested that the PEC revise the clinical rationale language on the PA forms to include information on the results of the CLASS study in regard to the use of COX-2 inhibitors in patients currently receiving low dose aspirin.

F. *Prior authorization of ciclopirox topical solution (Penlac Nail Lacquer) in the NMOP and retail network* – LTC Ed Zastawny (PEC) reported on a request from one of the MCSCs to add ciclopirox topical solution to the existing PA for antifungals for onychomycosis. Since other drugs for onychomycosis require prior authorization to ensure that they are used only when clinically appropriate (when a fungal infection is present), the Committee agreed that the same standard should be applied to ciclopirox. The committee voted to institute a PA for ciclopirox topical solution that requires confirmation of a fungal infection.

9. **STATUS OF LOW MOLECULAR WEIGHT HEPARINS (LMWHs) IN THE NMOP AND RETAIL NETWORK**

The Committee discussed the potential need to have LMWHs available through the NMOP. LMWHs are increasingly used in the outpatient sector and in some cases may be appropriately used for extended time periods (e.g., for pregnant women requiring anticoagulation). Dr. Rabie pointed out that there is now solid literature for 30 days of anticoagulation after joint replacement. While most clinicians switch patients from LMWHs to warfarin as soon as warfarin levels are therapeutic, some may opt to keep patients on enoxaparin or dalteparin for 30 days. The Committee asked the PEC to assess the opinions of providers about the necessity to have the LMWHs available through the NMOP.

10. **CONTROLLED DISTRIBUTION OF ALENDRONATE (FOSAMAX) 40 MG (FOR PAGET'S DISEASE)** – Alendronate 40 mg is no longer available through MTF pharmacies or retail network pharmacies, but is available through the NMOP. Most DoD beneficiaries who are age 65 and over cannot use the NMOP until 1 April 01. MAJ Bellemin reported that DSCP has worked out a procedure with Merck-Medco to honor prescriptions submitted by these DoD beneficiaries through their MTF pharmacies until they are eligible to use the NMOP on 1 April 01. Information about the interim procedure has been provided to the pharmacy consultants/specialty leaders for dissemination to MTF pharmacies.

11. **CONTROLLED DISTRIBUTION OF DOFETILIDE (TIKOSYN)** – Because of specialized educational requirements mandated by the FDA, dofetilide is only available for outpatient use through Stadtlander's Pharmacy/CVS Procare (which is a non-network pharmacy for DoD beneficiaries). COL Davies reported that the 50% copay penalty for using a non-network pharmacy can be waived retroactively, but the process is cumbersome. Attempts to establish a centrally funded process for supplying dofetilide to patients have thus far been unsuccessful.

12. **CONTROLLED DISTRIBUTION OF ETANERCEPT (ENBREL)**

Although a plan to supply etanercept only through the NMOP had been contemplated, LTC De Groff reported that etanercept would continue to be available through MTF pharmacies, retail network pharmacies, and the NMOP. Immunex and Wyeth/Ayerst have allotted supplies to MTF pharmacies based on historical usage data, so MTF pharmacies (unlike retail pharmacies) are not required to submit patient enrollment numbers to obtain etanercept. DoD beneficiaries can therefore obtain etanercept from MTF pharmacies even if they did not enroll with Immunex. However, unregistered patients may experience problems if they need to obtain etanercept from a source other than an MTF pharmacy.

13. **ADJOURNMENT –** The meeting adjourned at 1200 hours. The date and location for the next meeting have not been determined. All agenda items should be submitted to the co-chairs no later than 15 April 01.

<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 NMOP FORMULARY AND BCF

Generic name (Trade name; manufacturer)	**Indication, FDA approval date**	**NMOP Formulary Status**	**NMOP or retail network formulary restrictions**	**BCF Status**
Abacavir / lamivudine / zidovudine (Trizivir; Glaxo)	Approved 14 Nov 00 for use alone or in combination with other antiretroviral agents for treating HIV. Trizivir is intended only for patients whose regimen would otherwise include all three individual medications.	Added	**NMOP Preferred Drug Program** No **Quantity Limits** General rule applies **Prior Authorization** No	Not added
Sodium phosphate, dibasic, anhydrous / sodium phosphate monobasic, monohydrate (Visicol; Inkine)	Approved 21 September 2000 for cleansing of the bowel as a preparation for colonoscopy in adults 18 years of age or older.	Added	**NMOP Preferred Drug Program** No **Quantity Limits** General rule applies **Prior Authorization** No	Not added
Balsalazide disodium (Colazal; Salix)	Approved 18 Jul 00 for the treatment of mildly to moderately active ulcerative colitis. Oral prodrug of 5-aminosalicylic acid (5-ASA) in which the sulfapyridine moiety of sulfasalazine has been replaced with an inert carrier molecule.	Added	**NMOP Preferred Drug Program** No **Quantity Limits** General rule applies **Prior Authorization** No	Not added
Telmisartan/ HCTZ (Micardis HCT; Boehringer-Ingelheim)	Approved 11 Nov 00 for treatment of hypertension. As a fixed-dose combination, telmisartan/HCTZ is not indicated for initial therapy.	Added	**NMOP Preferred Drug Program** No **Quantity Limits** General rule applies **Prior Authorization** No	Not added
Tacrolimus ointment (Protopic; Fujisawa)	Approved 8 Dec 00 for short-term and intermittent long-term therapy in the treatment of patients with moderate to severe atopic dermatitis (AD) in whom the use of alternative conventional therapies is deemed inadvisable because of potential risks or in the treatment of patients who are not adequately responsive to or are intolerant of alternative conventional therapies. Indicated as 0.03% and 0.1% ointment for adults and only 0.03% ointment for children aged 2 to 15 years.	Added	**NMOP Preferred Drug Program** No **Quantity Limits** General rule applies; monitor quantities dispensed **Prior Authorization** No	Not added

APPENDIX A (CONTINUED): CONSIDERATION OF NEWLY APPROVED DRUGS FOR THE NMOP FORMULARY AND BCF

Generic name (Trade name; manufacturer)	**Indication, FDA approval date**	**NMOP Formulary Status**	**NMOP or retail network formulary restrictions**	**BCF Status**
Nateglinide (Starlix; Novartis)	Approved 22 Dec 00 as monotherapy in patients with type 2 diabetes mellitus whose hyperglycemia cannot be adequately controlled by diet and physical exercise, and who have not been chronically treated with other anti-diabetic agents (treatment-naïve patients). Nateglinide is also indicated for use in combination with metformin. Nateglinide may be added to but not substituted for metformin in patients already receiving metformin who still have inadequately controlled hyperglycemia. Patients receiving glyburide or sulfonylureas who have inadequately controlled hyperglycemia should not be switched to nateglinide, nor should nateglinide be added to their treatment regimen.	Added	**NMOP Preferred Drug Program** No **Quantity Limits** General rule applies **Prior Authorization** No	Not added

APPENDIX B: SUMMARY OF COST AVOIDANCE ASSOCIATED WITH THE NATIONAL MAIL ORDER PHARMACY (NMOP) PREFERRED DRUG PROGRAM

Summary of Switch Rates and Estimated Cost Avoidances FY 00

Non Preferred Drug	Preferred Drug	Switch Rate	Estimated Cost Avoidance	Total Attempted Provider Contacts	Estimated Cost Avoidance per Attempted Provider Contact
Cardizem CD, Dilacor XR, Cartia XT, Diltiazem XR	**Tiazac**	68%	$535,437	2904	$184
Procardia XL[1]	**Adalat CC**	53%	$313,918	1137	$276
Lodine XL, Relafen, Voltaren XR, Daypro, Naprelan	**Generic NSAIDs**	33%	$396,134	4118	$96
H2 Blockers	**Generic Ranitidine**	38%	$273,739	2485	$110
Vasotec[2]	**Zestril**	45%	$141,394	2741	$51
Famvir, Valtrex[3]	**Acyclovir**	24%	$6,783	1018	$7
Pletal[4]	**Pentoxifylline**	12%	$3424	280	$12
Ditropan XL, Detrol	**Generic Oxybutynin**	29%	$115,346	4003	$29
	Summary		**$1,779,392**	**17,668**	**$101**

Notes:

1. Calls for Procardia XL have diminished significantly (from 135 per month in Jun 00 to 7 per month in Dec 00), due to the introduction of generic equivalents for some strengths of Procardia XL. Procardia XL will be removed from the list of non-preferred drugs when generic equivalents are available for all strengths of Procardia XL.
2. Vasotec was removed from the list of non-preferred drugs when a generic equivalent became available at a competitive price in Dec 00.
3. At the May 00 meeting, the committee changed the criteria for Famvir and Valtrex so that calls would be made only for prescriptions written for chronic use (> 30 day supply). This change took effect 1 July 00.
4. Pletal was removed from the list of non-preferred drugs at the Aug 00 meeting (effective Sep 00), due to a low switch rate.

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* (See the 7 Feb 01 P&T Executive Council Minutes, Paragraph 10B and Appendix C)

      1) Clindamycin 150-mg capsules
      2) Loperamide 2-mg capsules
      3) Chlorhexidine gluconate 0.12% oral rinse (e.g., Peridex®, Periogard®, generics)
      4) Amoxicillin/clavulanic acid oral (tablets and suspension)
      5) Fluconazole oral, 150-mg tablets only. Includes only the single-dose regimen for treatment of vaginal candidiasis.
      6) Metoclopramide oral
      7) Mupirocin 1% ointment
      8) Metoprolol 50- and 100-mg oral. Does not include Toprol XL.
      9) Fluticasone oral inhaler
      10) Lactulose syrup
      11) Methotrexate oral
      12) Nitrofurantoin macrocrystals (generic equivalents to Macrodantin). Does not include Macrobid.

   B. *Changes and clarifications to the BCF* - None

2. **NMOP FORMULARY CHANGES**

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

      1) Abacavir / lamivudine / zidovudine (Trizivir; Glaxo)
      2) Sodium phosphate, dibasic, anhydrous / sodium phosphate monobasic, monohydrate (Visicol; Inkine)
      3) Balsalazide disodium (Colazal; Salix)
      4) Telmisartan/HCTZ (Micardis HCT; Boehringer-Ingelheim)
      5) Tacrolimus ointment (Protopic; Fujisawa)
      6) Nateglinide (Starlix; Novartis)

   B. *Exclusions from the NMOP Formulary* – None

   C. *Changes to the NMOP Preferred Drug Program* (See Appendix B)

      1) Procardia XL will be removed from the list of non-preferred drugs when generic equivalents are available for all strengths of Procardia XL.

      2) Vasotec was removed from the list of non-preferred drugs when a generic equivalent became available at a competitive price in Dec 00.

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

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

   A. A prior authorization that requires diagnostic verification of a fungal infection will be instituted for ciclopirox topical solution (Penlac Nail Lacquer) (See Paragraph 8F).

APPENDIX D: ITEMS TO BE ADDRESSED AT THE NEXT MEETING

1. *NMOP Preferred Drug Program Report* – See Paragraph 7 and Appendix B
2. *NMOP Prior Authorization Program Report* – See Paragraph 8
3. *Status of the Prior Authorization for Etanercept* – See Paragraph 8A3
4. *Status of Low Molecular Weight Heparins in the NMOP* – See Paragraph 9
5. *Controlled Distribution of Dofetilide (Tikosyn)* – See Paragraph 11
6. *Controlled Distribution of Etanercept (Enbrel)* – See Paragraph 12

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MCCS-GPE **7 Feb 2001**

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 convened at 0800 hours on 7 Feb 2001, at Ft Sam Houston, TX. The DoD P&T Executive Council is responsible for performing certain inherently governmental functions relevant to the DoD pharmacy benefits program. The Council focuses primarily on issues related to the Basic Core Formulary (BCF), national pharmaceutical contracts, and blanket purchase agreements. The DoD P&T Executive Council is comprised of federal employees who are members of the DoD P&T Committee.

2. **MEMBERS PRESENT:**

CDR Terrance Egland, MC	P& T Committee Co-chair
COL Daniel D. Remund, MS	P& T Committee Co-chair
COL Mark Nadeau, MC	Air Force (alternate)
COL (select) John R. Downs, MC	Air Force
MAJ George Jones, BSC	Air Force
CDR Matt Nutaitis, MC	Navy
MAJ Brett Kelly, MS	Army
CDR Robert Rist	Coast Guard
Ronald L. Mosier	Department of Veterans Affairs
LtCol Steven Humburg, MC	Health Affairs
MAJ Mickey Bellemin, BSC	Defense Supply Center Philadelphia

MEMBERS ABSENT:

COL Rosa Stith, MC	Army
LTC Judith O'Connor, MC	Army
CDR Kevin Cook, MSC	Navy
Joint Readiness Clinical Advisory Board Representative	

OTHERS PRESENT:

COL William Davies, MC	DoD Pharmacy Program Director, TMA
COL Mike Heath, MS	Army Pharmacy Consultant; Chair, DoD Pharmacy Board of Directors
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
CAPT Pat Welter	Navy Bureau of Medicine & Surgery
CDR Mark Brouker, MSC	DoD Pharmacoeconomic Center
LTC Don De Groff, MS	DoD Pharmacoeconomic Center
LtCol Ed Zastawny, BSC	DoD Pharmacoeconomic Center
LCDR Ted Briski	TRICARE Region 9 Lead Agent Office
MAJ Cheryl Filby, MS	Defense Supply Center Philadelphia
MAJ Barbara Roach, MC	DoD Pharmacoeconomic Center
Capt Krissa Crawford, BSC	Pharmacy Practice Resident, Wilford Hall Medical Center
HM3 Cory Beckner	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
Paul Vasquez	Defense Supply Center Philadelphia
Dana Dallas	Defense Supply Center Philadelphia

3. REVIEW MINUTES OF LAST MEETING

The minutes were approved as written.

4. ADVANCES IN MEDICAL PRACTICE (AMP) PROGRAM

Large budget shortfalls in the Defense Health Program jeopardize funding of the AMP program for FY 01. All AMP funds are currently "on hold" at TMA. Pharmacy will probably receive about $50 million if and when AMP funds are released. MTF pharmacies spent $12.1 million on AMP drugs in the first quarter of FY 01 (based on prime vendor data). Since expenditures for pharmaceuticals typically occur at the lowest rate during the first quarter of the fiscal year, total expenditures for AMP drugs will likely exceed $50 million in FY 01.

The Council considered a request from an MTF to add fluorodeoxyglucose (a radioactive fluoride used in positron emission tomography and single photon emission tomography) to the list of drugs covered by the AMP program. The Council denied the request because MTF expenditures for drugs currently covered by the AMP program will likely exceed the funds available for pharmacy in the AMP program.

5. NATIONAL PHARMACEUTICAL CONTRACTS

A. *Contract awards and renewals* – A joint VA/DoD single-source contract for clotrimazole 1% topical cream was awarded to Taro Pharmaceuticals with an effective date of 1 Feb 01. The joint VA/DoD single-source contract for acetaminophen 325 mg and 500 mg tablets announced at the last meeting became effective 1 Jan 01. MAJ Filby reported that the joint VA/DoD returned goods contract was awarded on 21 Jan 01 to Guaranteed Returns. LTC De Groff noted that 32 joint VA/DoD national contracts have been awarded, and approximately 25 more contracts are in various stages of development.

Information on national pharmaceutical contracts is available on the DSCP website (www.dmmonline.com).

B. *Financial impact of contracts* – COL Remund reported that the final estimate of MTF cost avoidance due to national pharmaceutical contracts was $65.2 million in FY 00, which equals 6.3% of the $1.03 billion that MTFs spent on pharmaceuticals. The weighted average percent reduction in cost for the drugs and drug classes affected by national pharmaceutical contracts was 25.3%. A summary of cost avoidance from national pharmaceutical contracts is provided in Appendix A.

C. *Status of solicitation for non-sedating antihistamine (NSA) contract* – The General Accounting Office (GAO) recently denied the only remaining protest of the solicitation for a joint VA/DoD "closed class" contract for a non-sedating antihistamine. The GAO denial of the protest opens the way for a contract to be awarded by the VA National Acquisition Center (NAC).

D. *Status of solicitation for oral contraceptive contracts* – The solicitation for joint VA/DoD single source contracts for four oral contraceptive products is scheduled to close on 23 Feb 01. The solicitation is for single sources of the following oral contraceptive products: 35 mcg ethinyl estradiol (EE) / 1 mg norethindrone; 35 mcg EE / 1 mg ethynodiol diacetate; 30/40/30 mcg EE / 0.05/0.075/0.125 mcg levonorgestrel; and 0.35 mg norethindrone.

E. *Status of potential contracting initiative for nasal corticosteroid inhalers* – DoD and VA officials will evaluate the potential for soliciting for a joint VA/DoD closed class contract for a high potency aqueous nasal corticosteroid inhaler after the VA has finished its clinical review of the drug class.

F. *Blanket purchase (BPA) agreements* – The Council wants to be more involved in the process of establishing BPAs in order to ensure that the provisions of a BPA support the Council's strategy for managing a given drug class. The Council also advocates the development of a more clearly defined process for establishing joint VA/DoD BPAs. The Council appointed a subcommittee to work on these issues. Subcommittee members are LTC De Groff, MAJ Filby, and LCDR Briski.

G. *Hepatitis A vaccine contract* – The United States Army Medical Materiel Center Europe (USAMMCE) reports that some facilities are buying Havrix instead of Vaqta, which is the contracted brand of hepatitis A vaccine. USAMMCE did not provide any information about why facilities are purchasing the non-contracted brand. The Council is unaware of any clinical reason for the facilities to use Havrix instead of Vaqta. The Council referred the issue back to DSCP for further investigation.

H. *Low molecular weight heparins* – The Council discussed the suitability of the low molecular weight heparin drug class for a contracting initiative. Additional information, including input from MTF providers, is needed to determine suitability for contracting.

6. **APPLICATIONS FOR DEA NUMBERS** – COL Humburg provided an update on online applications for DEA numbers.

7. **LEUTINIZING HORMONE RELEASING HORMONE (LHRH) AGONISTS** – A BPA makes goserelin available to MTFs at the VA national contract price in exchange for attainment of

an 80% overall share of the MTF prescriptions for LHRH agonists for prostate cancer. At the Nov 00 meeting the Council asked DSCP and the PEC to initiate an education/marketing campaign to ensure that goserelin achieves the market share required by the BPA. CAPT Torkildson reported that the following actions were taken since that meeting:

- Information regarding the Council's decision and the BPA was published in the P&T Executive Council minutes.
- Specialty leaders for Urology in each service were notified of the BPA and informed of the opportunity for cost savings. Information was forwarded to urologists.
- An article was published in the Dec 00 edition of the *PEC Update.*
- Information about the goserelin BPA was provided to the pharmacy and/or urology departments at MTFs with high leuprolide usage.

The Council reviewed MTF prescription data for LHRH agonists, but concluded that it was too early to accurately discern the effect of the BPA on LHRH agonist usage and whether MTFs are on track to achieve the 80% market share for goserelin by 1 Aug 00.

The Council was informed that DSCP recently accepted a BPA from TAP Pharmaceuticals that lowered the price of leuprolide, but still leaves leuprolide with a higher price per dose than goserelin. The Council concluded that the goserelin BPA offers the best value for the MHS. The Council reaffirmed its desire to have goserelin reach an 80% market share by 1 Aug 00 and advised the PEC to continue educational efforts to attain that goal.

8. **DRUG USAGE NOT CAPTURED IN CHCS** – As part of its analysis of LHRH agonist usage, the PEC compared the quantity of LHRH agonists purchased through the prime vendor to the quantity dispensed on outpatient prescriptions. The quantity purchased significantly exceeded the quantity dispensed at 10 MTFs. The discrepancy between the purchase data and the dispensing data is most likely due to the fact that LHRH agonists are dispensed to outpatient clinics through bulk drug orders at some MTFs. Because the agent is administered to the patient in the clinic, the drug usage is not recorded in CHCS. Outpatient drug usage that is not recorded in CHCS is omitted from clinical screening within CHCS and through the Pharmacy Data Transaction Service (PDTS). The ability of the CHCS and PDTS clinical screening processes to improve patient safety is diminished when outpatient drug usage is not recorded in CHCS. This issue was referred to LTC DeGroff, PDTS Functional Program Manager, and COL Heath, chairman of the DoD Pharmacy Board of Directors.

9. **MTF REQUESTS FOR BCF CHANGES**

   A. *Request to remove methylphenidate extended-release (Concerta) from the BCF* – An MTF requested that methylphenidate extended-release (Concerta) be removed from the BCF because:

   - They could find no literature to indicate that Concerta is a superior product to those already available.
   - Concerta is not the only agent that can be dosed prior to the child leaving for school without requiring a noon dose.
   - Having another Schedule II item is always an issue.

According to a recent New Product Bulletin from the American Pharmaceutical Association (APhA), the duration of action is about 12 hours for Concerta, compared to 3 to 6 hours for methylphenidate immediate-release tablets and about 8 hours for the sustained release tablets. To the extent that a longer duration of action is desirable, Concerta might be considered superior to other currently available methylphenidate products.

A PEC analysis of MTF prescriptions for a random sample of patients under the age of 18 who received more than one prescription for sustained-release methylphenidate during FY 00 revealed the following:

- 60% (116/193) of the patients received another medication for ADHD in addition to sustained-release methylphenidate.
- 40% (78/193) of the patients were prescribed a midday dose of either sustained-release methylphenidate or another medication for ADHD.

Although methylphenidate sustained release tablets should theoretically obviate the need for a midday dose, MTF prescription data show that midday doses are frequently prescribed for patients taking methylphenidate sustained release tablets. The Council voted to keep Concerta on the BCF.

B. *Request to add gatifloxacin (Tequin) and remove levofloxacin (Levaquin) from the BCF* – An MTF pharmacy chief suggested that the addition of levofloxacin to the BCF may have been based on (1) an incorrect price for gatifloxacin, and (2) inadequate consideration of *S. pneumoniae* MICs and use in sexually transmitted diseases.

The Council was aware at the Nov 00 meeting that both levofloxacin and gatifloxacin were available for $2.00 per daily dose through BPAs. The Council also considered levofloxacin and gatifloxacin to be very similar in safety, tolerability and efficacy. Levofloxacin accounted for nearly 70% of all fluoroquinolone prescriptions dispensed at MTFs, while gatifloxacin accounted for less than 1% of fluoroquinolone prescriptions.

As requested by the Council, DSCP obtained a revised BPA that makes it easier for MTFs to obtain levofloxacin at the BPA price. The revised BPA offers levofloxacin 250 mg and 500 mg to all MTFs at an upfront price of $2.00 per tablet. Continuation of the BPA price is contingent upon levofloxacin achieving either (1) an 80% aggregate DoD market share within 6 months, or (2) a 50% market share at individual MTFs. Market share will be based on patient days of therapy and will be calculated from USPD prescription data.

The revised BPA achieves the objective of making it easier for MTFs to obtain levofloxacin at the BPA price, since MTFs are no longer responsible for individually monitoring drug usage to meet market share requirements. In addition, use of prescription data eliminates the problem of prime vendor purchases of ciprofloxacin being included in the denominator for calculating levofloxacin market share. However, some of the provisions in the BPA were unacceptable to the Council. The Council asked DSCP to revise the BPA to eliminate the unacceptable provisions.

The Council was also informed that a new incentive price agreement offers gatifloxacin to MTFs at a price of $1.90 per daily dose. The incentive price is contingent on gatifloxacin having a preferred or co-preferred formulary position at an individual MTF.

The Council voted to keep levofloxacin on the BCF. The fluoroquinolone class remains open on the BCF, so MTFs may have other fluoroquinolones on their formulary in addition to levofloxacin.

C. *Request to remove divalproex ER (Depakote ER) from BCF* – An MTF pharmacist asserted that Depakote ER (which is dosed once daily) offers no advantages over Depakote (which is dosed twice daily) because there are no data to prove better compliance.

All oral dosage forms and strengths are generally included for a drug listed on the BCF. The DoD P&T Committee may specifically omit a dosage form or strength from the BCF if it is excessively expensive compared to the other dosage forms/strengths, or if impending availability of a generic equivalent makes it inadvisable to include a given dosage form. Depakote ER is priced essentially the same as Depakote. The Council voted to keep Depakote ER on the BCF.

10. **BASIC CORE FORMULARY REVIEW**

A. *BCF overview and analysis* – The Council reviewed the objective of the BCF and factors that are considered in selecting drugs for the BCF (see Appendix B). The PEC recommended drugs for addition to the BCF based on the following information and analyses:

1) An analysis of USPD data showed that 72.6% of the prescriptions filled at MTF pharmacies in FY 00 were filled with drugs that were on the BCF at the end of FY 00. Prescriptions for most over-the-counter drugs were excluded from the analysis because they generally are not eligible for inclusion on the BCF. The analysis did not characterize second-generation antihistamines, low molecular weight heparins, leukotriene antagonists, and estrogenic vaginal creams as BCF drugs—even though the BCF requires MTFs to have at least one agent from each of those drug classes on the MTF formulary.

2) A frequency distribution of prescriptions filled at MTFs for BCF and non-BCF drugs that was generated from USPD data.

3) A survey of MTFs to determine the MTF formulary status for 98 drugs that are not currently included on the BCF.

4) Input from MTF providers.

5) Drug usage and cost trends from prime vendor and USPD data.

B. *Addition of drugs to the BCF* – The Council was forced to take a conservative approach in adding drugs to the BCF because of the uncertain funding situation for the Defense Health Program in FY 01. The Council added 12 drugs to the BCF, which are listed in Appendix C. [NOTE: A comprehensive list of all BCF and NMOP formulary changes is provided in an appendix to the 8 Feb 01 DoD P&T Committee minutes.]

C. *Drugs not added to the BCF* – The Council considered clinical information and usage data regarding gabapentin, COX-2 inhibitors, and dihydropyridine calcium channel blockers. The Council did not add any of these drugs to the BCF.

D. *Ongoing review* – The PEC is reviewing topical corticosteroids, benzodiazepines, and medications for acne and overactive bladder. Information on these drugs will be presented at the next meeting of the P&T Executive Council.

E. *Status of lancets on the BCF* – A Council member asked why lancets are not included on the BCF. The Council tabled this issue until the next meeting.

11. The meeting adjourned at 1230 hours. The date and location of the next meeting are to be determined.

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

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

Appendix A: Cost Avoidance in DoD MTFs Due to National Pharmaceutical Contracts, FY 00

Estimated Cost Avoidance in DoD MTFs Due to National Pharmaceutical Contracts, Fiscal Year 2000

Drug/Drug Class	Contract Start Date	Weighted Average Price/Unit Before Contracted	Theoretical FY 00 Cost If Not Contracted	FY 00 Actual Cost	Cost Avoidance	Percent Reduction in Cost
Statins	1-Oct-99	$0.961874	$94,988,500	$72,672,448	$22,316,052	23.49%
PPIs	1-Oct-99	$1.681407	$97,608,455	$78,179,686	$19,428,769	19.90%
Lisinopril	1-Aug-99	$0.284396	$22,410,939	$12,338,214	$10,072,726	44.95%
Diltiazem	15-Dec-98	$0.631469	$13,077,589	$6,118,739	$6,958,850	53.21%
Ranitidine	16-Nov-98	$0.066602	$3,819,158	$1,956,040	$1,863,118	48.78%
Hepatitis A	18-Sep-99	$16.981597	$8,221,080	$6,546,563	$1,674,517	20.37%
Albuterol	16-Nov-98	$3.297032	$2,882,500	$1,932,971	$949,529	32.94%
Timolol Gel	14-Jan-00	$14.598153	$952,836	$417,571	$535,265	56.18%
Verapamil	20-Aug-99	$0.125912	$2,358,022	$1,804,406	$553,616	23.48%
Cimetidine	16-Nov-98	$0.072763	$833,304	$540,391	$292,913	35.15%
Terazosin	5-Sep-00	$0.459093	$726,193	$539,565	$186,628	25.70%
Captopril	18-Oct-99	$0.036173	$313,233	$171,569	$141,664	45.23%
Nortriptyline	15-Oct-99	$0.049281	$311,276	$227,111	$84,165	27.04%
Gemfibrozil	1-Jan-00	$0.077935	$995,172	$914,650	$80,522	8.09%
Naproxen	3-Jul-00	$0.069829	$752,114	$673,203	$78,911	10.49%
Amoxicillin	7-Aug-99	$0.040549	$560,140	$499,419	$60,721	10.84%
Insulin Syringes	1-May-00	$0.098121	$430,084	$408,406	$21,678	5.04%
Timolol Drops	14-Jan-00	$2.795264	$195,968	$162,419	$33,548	17.12%
Nicotine Patches	1-Jun-00	$2.567746	$518,454	$460,290	$58,163	11.22%
Levobunolol	14-Jan-00	$4.641527	$54,385	$37,522	$16,863	31.01%
Fluocinonide	1-Sep-99	Cream $1.816402 Oint $6.210282 Sol $6.422653	$370,547	$355,800	$14,747	3.98%
Prazosin	1-Nov-99	$0.032916	$132,685	$118,531	$14,153	10.67%
Amantadine	28-Aug-99	$0.063871	$61,008	$53,950	$7,058	11.57%
Naproxen Sodium	3-Jul-00	$0.073176	$47,017	$48,695	($1,678)	-3.57%
Salsalate	15-Mar-00	$0.026462	$79,751	$87,525	($7,774)	-9.75%
Insulin	1-Nov-99	$5.292812	$4,818,894	$5,071,036	($252,142)	-5.23%
Acyclovir	1-Oct-00	$0.121623			NA	NA
Azathioprine	1-Oct-00	$0.477152			NA	NA
Hydroxyurea	1-Oct-00	$0.295324			NA	NA
Pentoxifylline	1-Oct-00	$0.182262			NA	NA
Rifampin	1-Oct-00	$0.566776			NA	NA
Sucralfate	1-Oct-00	$0.198476			NA	NA
Acetaminophen	1-Jan-01				NA	NA
TOTAL FY00			**$257,519,303**	**$192,336,719**	**$65,182,584**	**25.31%**

Explanation of Cost Avoidance Calculations: Cost avoidance equals the difference between (1) the theoretical cost that would have occurred in FY 00 if a contract had not existed, and (2) the actual cost that was incurred in FY 00 for the "market basket" of drugs that pertains to each contract. The theoretical cost that would have occurred in FY 00 if a contract had not existed was estimated by multiplying the weighted average price/unit that existed before the contract took effect by the quantity purchased in FY 00 after the contract was in effect. The "market basket" of drugs includes both the contracted and the non-contracted drugs that pertain to a given contract. For example, the cost avoidance for statins takes into account the expenditures for all six statins, not just the two contracted statins.

Appendix B: Objective of the Basic Core Formulary and Factors Considered in Drug Selection

A. *Objective of the Basic Core Formulary (BCF)*

Ensure uniform availability of cost-effective pharmaceuticals at MTF pharmacies to meet the majority of patients' primary care needs

B. *Selecting drugs for the BCF*

Compare the drug to other agents in the class or other agents that are used for a given disease/condition, based on the following factors:

Safety

Tolerability

Efficacy / Effectiveness

Price / Cost

Other factors, including but not limited to:

- Place in therapy / clinical niche
- Interchangeability of drugs in the class
- Variability in patient response to drugs in the class
- MTF provider opinions/preferences
- Market share trends within the drug class
- Percentage of MTFs that have the drug on formulary
- Potential for inappropriate use
- Patent expirations and impending availability of generic equivalents

Appendix C: Drugs Added to the BCF

Drug	Factors Considered Safety, tolerability, efficacy, price, and other factors (STEPO) relative to other drugs in the same class and/or current BCF items, if any	Percentage of MTFs reporting drug on formulary
Clindamycin 150-mg capsules	S/T/E: Safe and effective for treatment of commonly encountered acute infections. P: Generics available. Capsule prices range from $0.28 to $1.15 (branded 300-mg capsule) O: Class not represented on current BCF. Alternative for skin, soft-tissue, and respiratory tract infections in PCN allergic patients. Needed for treatment of polymicrobial infections where anaerobes are suspected.	Unknown
Loperamide 2-mg capsules	S/T: Safer than diphenoxylate/atropine (e.g., Lomotil). Does not interact with MAO inhibitors or CNS depressants. Does not cause physical dependence. Less drowsiness and sedation compared to diphenoxylate/atropine. E: Efficacy similar to diphenoxylate/atropine. P: DAPA price = $0.046 per capsule, compared to $0.017 per tablet for diphenoxylate/atropine O: Available on a high number of local formularies. A non-scheduled alternative to diphenoxylate/atropine (will not add to administrative burden).	98.7% (155/157)
Chlorhexidine gluconate 0.12% oral rinse (Peridex®, Periogard®, generics) – used for treating gingivitis	S/T: No systemic effects (topical application). Potential cosmetic concerns include staining of the tooth surfaces, restorations, and dorsum of the tongue. Occasional alterations in taste perception. E: No available published literature that treating gingivitis decreases tooth loss. There are conflicting reports on the relationship between periodontal disease and coronary heart disease in men. P: Price ranges from $2.44 to $3.00 for 473 mL bottles O: No similar agents are available on the BCF Satisfies an unique therapeutic niche Dental consultants agreed that this product belongs on the BCF Space limitations may be a concern in smaller MTFs	96.8% (152/157)
Amox/clav (Augmentin) tablets and suspension	S/T/E: Widely used agent proven safe and effective in broad range of infectious processes. P: Already available at nearly all MTFs, so minimal cost impact. O: Class not represented on BCF. Widely used to treat respiratory tract infections and otitis media where penicillinase-producing organism is known or suspected.	Tablets - 96.8% (152/157) Susp – 97.5% (153/157)
Fluconazole oral, 150-mg tablets only	S/T/E: Proven safe and effective for treatment of vaginal candidiasis. P: $6.63 to $6.89 per treatment. OTC cream DAPA price range from $3.35 to $4.42 per 45gm tube. O: No alternatives currently listed on the BCF. As effective as OTC vaginal creams. Offers advantage of single dose therapy and ease of administration.	96.8% (152/157)

Drug	Factors Considered Safety, tolerability, efficacy, price, and other factors (STEPO) relative to other drugs in the same class and/or current BCF items, if any	Percentage of MTFs reporting drug on formulary
Metoclo-pramide oral	S/T: Metoclopramide is well tolerated with CNS side effects of drowsiness, fatigue and lassitude occurring in roughly 10% of patients at normal doses. Extrapyramidal and/or dystonic reactions are rare, occurring in about 0.2% of patients. E: Effective in the treatment of diabetic gastroparesis for which there is no other treatment. P: Price is less than $0.01 per tablet. O: No similar product on the BCF	Metoclopramide 95.5% (150/157)
Mupirocin 1% ointment	ST: Only safety issue would be in patients with renal failure who need to use it on a large open wound area; otherwise mupirocin is not absorbed systemically. No significant tolerability issues. E: Bacitracin nearly 100% failure rate for impetigo. Oral erythromycin now > 50% failure rate due to resistance. Nearly 100% successful treatment of impetigo with mupirocin or cephalexin. Using mupirocin avoids problems related to systemic therapy. Studies were done at Tripler. P: DAPA prices: ointment $22.03 per 22gm tube; cream $16.24 per 15 gm tube, $27.56 per 30 gm tube; nasal ointment $29.57 (box of 10, 1gm tube) O: Nothing similar in this category of therapy on BCF. On the VA formulary with restrictions. Many schools and day care centers will not allow children with impetigo to return until they have been treated.	Mupirocin oint. – 143/157 – 91.1%
Metoprolol 50mg, 100mg oral (Toprol XL is not included in this listing for metoprolol)*	S: Safe when used as directed. Avoid in patients with severe reactive airway disease, concurrent negative inotropic agents, severe or unstable heart failure. T: Well tolerated. β-1 selective agent may minimize β2 blockade related adverse effects (bronchospasm). Selectivity is lost with higher doses. E: Effective in treating HTN, angina, post-MI, selected CHF patients (stable NYHA II and NYHA III). Proven mortality benefit in all these conditions. Usually dosed BID. Can be used QD for HTN in some patients. P: Inexpensive. Metoprolol 50mg generic - $0.02-0.06, Metoprolol 100mg generic - $0.03-0.05, Toprol XL® 50mg - $0.46, Toprol XL® 100mg - $0.92 (Dec 2000 DAPA prices). Toprol XL® 25mg scored tablet – submitted for FDA approval for stable NYHA II-III CHF patients – release date unknown. O: Proven mortality benefit in several indications. Want to encourage use, esp in post-MI patients (decreases mortality and is a HEDIS measure). **Toprol XL® was excluded because there are insufficient clinical advantages to justify the incremental cost compared to immediate release metoprolol.*	Metoprolol – 142/157 – 90.4% Toprol XL – 7/157 – 4.5%

Drug	Factors Considered Safety, tolerability, efficacy, price, and other factors (STEPO) relative to other drugs in the same class and/or current BCF items, if any	Percentage of MTFs reporting drug on formulary
Fluticasone oral inhaler (For complete analysis and clinical information, see Review of Orally Inhaled Corticosteroids, Nov 00 DOD P & T Committee Meeting)	S/T: Fluticasone is equal in safety to other inhaled corticosteroids (ICS) on the market. Adverse reactions appear to be similar to the other available ICS. E: When given in equipotent doses, all the ICS appear to have equal efficacy. Fluticasone, like budesonide, is a high potency ICS that may require fewer puffs per day to achieve control of asthma. P: DAPA prices - 44 mcg MDI $19.88 110 mcg MDI $29.03, 220 mcg MDI $50.65, 50 mcg DPI $21.32, 100 mcg DPI $27.95, 250 mcg DPI $35.98 O: There are no high potency ICS on the BCF. Of the two high potency ICS, fluticasone has a significant share of the market compared to budesonide (39% versus 3.5%). The two high potency ICS are not interchangeable. Budesonide is a dry powder inhaler (DPI); fluticasone is available as both a DPI and a metered dose inhaler (MDI). Given the difference in dosage forms, significant and costly patient education would be required to switch patients currently on fluticasone to budesonide. Budesonide is less desirable than fluticasone because providers report that patients have difficulty in administering the correct dose because of the lack of tactile feedback. Breath actuation with budesonide may be particularly difficult for children.	135/157 (86.0%)
Lactulose syrup	ST: No significant safety issues. Better tolerated than other 2 maintenance therapies recommended for children (mineral oil, magnesium salts). Common side effects (flatulence, belching, abdominal distension, abdominal pain) generally mild. E: Several clinical trials have demonstrated significant increase in stool frequency, weight, volume, and water content compared to placebo. P: DAPA price $3.97/480 ml vs. $17.92 approximate retail price O: Constipation prevalent in pediatric population. Adult therapies not generally used in children	Unknown
Methotrexate oral	ST: Substantial toxicity, low therapeutic index. Not possible to logically compare to other agents. E: No equivalent antineoplastic agent on BCF. No other DMARDs on BCF. Efficacy as antineoplastic agent and immunosuppressive agent clearly demonstrated. P: Generic product available. DAPA price $0.12/tablet; 2.5-10 fold lower than approximate retail price O: Availability of best alternative DMARD (etanercept) greatly limited. Rheumatrex dose packs significantly more expensive than bulk tablets.	80.9% (127/157)

Drug	Factors Considered Safety, tolerability, efficacy, price, and other factors (STEPO) relative to other drugs in the same class and/or current BCF items, if any	Percentage of MTFs reporting drug on formulary
Nitrofurantoin macrocrystals (generic equivalents to Macrodantin) Macrobid is not included*	S/T/E: Specifically for the treatment and suppression of UTI. P: Generics available Price range from $0.07 to $0.87/dose. O: Recommended as one of primary agents in DOD Acute Dysuria or Urgency in Women Guideline. **MacroBid â was excluded because it offers no significant clinical advantage over available generic products.*	Capsules – 72.6% (114/157) Macrocrystals – 79% (124/157) Susp - Unknown