Post-Implementation Review
Prostate Cancer Agents

Review: February 2019
Implementation: 31 July 2019
## DoD UF Class: Oncological Agents
### Subclasses: CYP-17 Inhibitors & 2nd-Gen Antiandrogens
### Current Formulary Status (July 2020)

<table>
<thead>
<tr>
<th>Basic Core Formulary (BCF)</th>
<th>Uniform Formulary (UF)</th>
<th>Non-formulary (NF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTFs must have on formulary</td>
<td>CYP-17 Inhibitors (CYP17)</td>
<td>N/A – No CYP-17 Inhibitors or 2nd-Gen Antiandrogens agents are designated basic core formulary</td>
</tr>
<tr>
<td></td>
<td>Step-Preferred:</td>
<td>N/A – No CYP-17 Inhibitors or 2nd-Gen Antiandrogens agents are designated non-formulary</td>
</tr>
<tr>
<td></td>
<td>• abiraterone acetate micronized (Yonsa)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-Step-Preferred:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• abiraterone acetate (generic)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• abiraterone acetate (Zytiga)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2nd-Gen Antiandrogens (2nd-Gen AA)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Step-Preferred:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• enzalutamide (Xtandi)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-Step-Preferred:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• apalutamide (Erleada)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• darolutamide (Nubeqa) – Nov 2019</td>
<td></td>
</tr>
</tbody>
</table>

*abiraterone acetate 250 mg (generic) no longer requires trial of Yonsa first – Nov 2019
  • abiraterone acetate 500 mg (Zytiga) must have a trial of Yonsa OR generic abiraterone acetate 250 mg first AND reason stated why 500 mg is needed

apalutamide (Erleada) and darolutamdie (Nubeqa) are UF, but non-step preferred
  • must have a trial of enzalutamide (Xtandi) first

Prior Authorization (PA) and Quantity Limits apply to all CYP-17 Inhibitors and 2nd-Gen Antiandrogens
## Drugs in Subclasses: **CYP17** and 2nd-Gen AA

<table>
<thead>
<tr>
<th>Generic/Brand</th>
<th>MOA</th>
<th>FDA Approval Date</th>
<th>Dosage</th>
<th>Indication</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>abiraterone acetate (Zytiga)</td>
<td>Androgen Synthesis Inhibitor (CYP17)</td>
<td>Apr 2011</td>
<td>1000 mg once daily with prednisone</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>abiraterone acetate micronized (Yonsa)</td>
<td>Androgen Synthesis Inhibitor (CYP17)</td>
<td>May 2018</td>
<td>500 mg once daily with methylprednisolone</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>enzalutamide (Xtandi)</td>
<td>Androgen Receptor Inhibitor</td>
<td>Aug 2012</td>
<td>160 mg once daily</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>apalutamide (Erleada)</td>
<td>Androgen Receptor Inhibitor</td>
<td>Feb 2018</td>
<td>240 mg once daily</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>darolutamide (Nubeqa)</td>
<td>Androgen Receptor Inhibitor</td>
<td>Jul 2019</td>
<td>600 mg BID</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

**Indication**
- nmHSPC = non-metastatic hormone-sensitive (also known as castration-sensitive or castration-naïve) prostate cancer
- nmCRPC = non-metastatic castration-resistant prostate cancer
- mHSPC = metastatic hormone-sensitive (also known as castration-sensitive or castration-naïve) prostate cancer
- mCRPC = metastatic castration-resistant prostate cancer

**Other**
- X = original FDA indication from 2015 class review
- X = new FDA indication since 2015 class review (added 2018 & 2019)
- O = guideline driven off-label use

*GnRH = gonadotropin-releasing hormone (Patient must be receiving a GnRH analog concomitantly with all five drugs listed above OR have had a bilateral orchiectomy)*
Overall Clinical Conclusions (Feb 2019) for **CYP17** and **2nd-Gen AA** Agents

- **Subclasses have two different mechanisms of action**
  - **CYP17 subclass:**
    - same molecular entity: abiraterone acetate
    - no difference in guideline driven recommendations between agents (both agents recommended in all non-localized forms of prostate cancer)
    - no clinically meaningful difference in safety between abiraterone agents; monitor patients for mineralocorticoid excess (BP, K⁺, and edema), adrenocortical insufficiency, and hepatotoxicity
  - **2nd-Gen AA subclass:**
    - only enzalutamide (Xtandi) is recommended for use in mCRPC; both enzalutamide (Xtandi) and apalutamide (Erleada) are recommended in nmCRPC
    - comparative effectiveness of enzalutamide (Xtandi) and apalutamide (Erleada), when used in nmCRPC, cannot be determined at this time
    - similar side effect profiles; PROSPER trial in mCRPC with enzalutamide (Xtandi) showed disproportionate cardiac side effect/death rate vs placebo, but this was not reproduced in other studies with enzalutamide (Xtandi)
- **Ongoing trials for combination CYP17 & 2nd-Gen AA agents in mCRCP**
- **Pipeline shows 1 agent in each subclass in trials**
- **No head-to-head comparative trials for any of these agents in either subclass**
- **Need 1 formulary agent from each subclass**
Selected Slides From February 2019 Cost Review
Prostate Cancer agents
Utilization and cost, one year

CYP17 inhibitor

- Number of 30DE: 10,205
- Net MHS Cost: $52.1M

2nd gen AA

- Number of 30DE: 10,730
- Net MHS Cost: $42.5M

**CYP17 subclass**

<table>
<thead>
<tr>
<th>One Year</th>
<th>Number of 30DE</th>
<th>Net MHS Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mail</td>
<td>4,600</td>
<td>$20.7M</td>
</tr>
<tr>
<td>MTF</td>
<td>1,200</td>
<td>$5.3M</td>
</tr>
<tr>
<td>Retail</td>
<td>4,400</td>
<td>$26.1M</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10,200</strong></td>
<td><strong>$52.1M</strong></td>
</tr>
</tbody>
</table>

- abiraterone (Zytiga 250mg, 500mg)
- abiraterone (generic for Zytiga 250mg)
- abiraterone submicronized (Yonsa, 125mg)

**2nd-Gen AA subclass**

<table>
<thead>
<tr>
<th>One Year</th>
<th>30DE</th>
<th>Net MHS Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mail</td>
<td>6,100</td>
<td>$23.6M</td>
</tr>
<tr>
<td>MTF</td>
<td>1,400</td>
<td>$6.1M</td>
</tr>
<tr>
<td>Retail</td>
<td>3,300</td>
<td>$12.8M</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10,800</strong></td>
<td><strong>$42.5M</strong></td>
</tr>
</tbody>
</table>

- apalutamide (Erleada)
- enzalutamide (Xtandi)

Source: PDTS, includes OHI; Dec 2017 – Nov 2018
From Feb 2019 review

Budget Impact Analysis (BIA) – CYP17
Outlook – One Year

Average cost per month: $5,100

Baseline = $60.2
↓ $7.2M

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Mail</th>
<th>MTF</th>
<th>Retail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario 1</td>
<td>20.1</td>
<td>6.0</td>
<td>26.9</td>
</tr>
<tr>
<td>Scenario 2</td>
<td>23.3</td>
<td>7.5</td>
<td>27.3</td>
</tr>
<tr>
<td>Scenario 3</td>
<td>24.0</td>
<td>7.1</td>
<td>29.0</td>
</tr>
<tr>
<td>Scenario 4</td>
<td>24.0</td>
<td>7.1</td>
<td>29.0</td>
</tr>
<tr>
<td>Scenario 5</td>
<td>29.3</td>
<td>9.4</td>
<td>30.0</td>
</tr>
</tbody>
</table>

CYP17 agents: abiraterone (Zytiga 250mg and generic, 500mg brand); abiraterone submicronized (Yonsa, 125mg)
The budget impact analysis provides relative cost estimates for various formulary placement options of agents in the class.

CYP17 agents: abiraterone (Zytiga 250mg and generic, 500mg brand); abiraterone submicronized (Yonsa, 125mg)
Budget Impact Analysis – 2nd-Gen AA
Outlook – One Year

Average cost per month: $3,900

Baseline = $50.1M

Δ $1.1M

<table>
<thead>
<tr>
<th>Scenario 6</th>
<th>Scenario 7</th>
<th>Scenario 8</th>
<th>Scenario 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>49.0</td>
<td>49.0</td>
<td>59.9</td>
<td>59.9</td>
</tr>
<tr>
<td>6.3</td>
<td>6.3</td>
<td>8.0</td>
<td>8.0</td>
</tr>
<tr>
<td>27.9</td>
<td>27.9</td>
<td>34.0</td>
<td>34.0</td>
</tr>
<tr>
<td>14.8</td>
<td>14.8</td>
<td>17.8</td>
<td>17.8</td>
</tr>
</tbody>
</table>

2nd-Gen AA: apalutamide (Erleada); enzalutamide (Xtandi)
Committee Recommendations

- Formulary Status Recommendations:
  - Step-preferred/Tier 1: **Yonsa** (CYP17); **Xtandi** (2nd Gen AA)
  - UF/non-step-preferred: **Zytiga** (CYP17); **Erleada** (2nd Gen AA)

- CYP17: No grandfathering
- 2nd Gen AA: Grandfathered

- CYP17 prior authorization criteria required Yonsa step-preferred, then abiraterone 250mg before abiraterone 500mg
Post-implementation results
Implemented Aug 2019
Prostate Cancer Agents
30-Day Equivalents

CYP17: abiraterone (Zytiga) and abiraterone submic (Yonsa)

2nd-Gen AA: apalutamide (Erleada) and enzalutamide (Xtandi)

6% increase in 30DE when comparing pre- and post- periods

Source: PDTS. Excludes patients with other health insurance.
CYP17 Subclass
30-Day Equivalents

Modified the Yonsa step related to abiraterone 250mg

Implementation date

Source: PDTS. Excludes patients with other health insurance.
CYP17 Subclass
30-Day Equivalents

- **Yonsa**
- **Zytiga**
- **Abiraterone (gen)**
- **Abiraterone 125 and 250 combined**

**Source:** PDTS. Excludes patients with other health insurance.
2nd-Gen AA Subclass
30-Day Equivalents

Source: PDTS. Excludes patients with other health insurance.
Prostate Cancer Agents
Net MHS Cost

CYP17: abiraterone (Zytiga) and abiraterone submic (Yonsa)
2nd-Gen AA: apalutamide (Erleada) and enzalutamide (Xtandi)

Source: PDTS. Excludes patients with other health insurance.
Prostate Cancer Agents
Net MHS Cost

CYP17: abiraterone (Zytiga) and abiraterone submic (Yonsa)
2nd-Gen AA: apalutamide (Erleada) and enzalutamide (Xtandi)

Source: PDTS. Excludes patients with other health insurance
Prostate Cancer Agents

Net MHS Cost

CYP17: abiraterone (Zytiga) and abiraterone submic (Yonsa)

2nd-Gen AA: apalutamide (Erleada) and enzalutamide (Xtandi)

Six Months Pre: $59.8M
Six Months Post: $54.6M

$5.3M for the six-month periods pre- and post-implementation, even with 6% workload increase

Source: PDTS. Excludes patients with other health insurance
Prostate Cancer Agents
Summary of Cost and Workload (30DE)

Net MHS Cost | 30-Day Equivalents

$10.5M | 2,566 ↑13.3%
$9.2M | 1,970 30DE
$10.5M | 2,265 30DE

Potential FY20 spend at current utilization:
Using pre-review cost per month: $133.2M
Using post-review cost per month: $117.3M

Source: PDTS. Excludes patients with other health insurance
Prostate Cancer Agents
UF Class Review Summary

- The prostate cancer agents class review resulted in **significant** and **sustained cost avoidance** for the MHS
  - Patient count and workload were not negatively impacted
  - Cost avoidance exceeded the conservative BIA estimate
- MHS spend was ↓$5.3M in first six months post-implementation
  - FY20 potential savings of $15.9M
- Savings from UF class reviews can vary based on competition, comparator interchangeability, and other market factors
- MTF takeaways:
  - Review quarterly DoD P&T Committee minutes, and results of other post-meeting reviews, at [http://health.mil/pandt](http://health.mil/pandt)
  - Formulary management tools can have a huge impact, everyone plays a role in successful implementation