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# Post-Implementation Review Prostate Cancer Agents

Review: February 2019

Implementation: 31 July 2019

**DoD UF Class: Oncological Agents**  
**Subclasses: CYP-17 Inhibitors & 2<sup>nd</sup>-Gen Antiandrogens**  
**Current Formulary Status (July 2020)**



<b>Basic Core Formulary (BCF)</b> <b>MTFs <u>must</u> have on formulary</b>	<b>Uniform Formulary (UF)</b> <b>MTFs <u>may</u> have on formulary</b>	<b>Non-formulary (NF)</b> <b>MTFs <u>must not</u> have on formulary</b>
<p>N/A – No <b>CYP-17 Inhibitors</b> or <b>2<sup>nd</sup>-Gen Antiandrogens</b> agents are designated basic core formulary</p>	<p><b>CYP-17 Inhibitors (CYP17)</b></p> <p><b><u>Step-Preferred:</u></b></p> <ul style="list-style-type: none"> <li>abiraterone acetate micronized (Yonsa)</li> </ul> <p><b><u>Non-Step-Preferred:</u></b></p> <ul style="list-style-type: none"> <li>abiraterone acetate (generic)*</li> <li>abiraterone acetate (Zytiga)</li> </ul> <p><b>2<sup>nd</sup>-Gen Antiandrogens (2<sup>nd</sup>-Gen AA)</b></p> <p><b><u>Step-Preferred:</u></b></p> <ul style="list-style-type: none"> <li>enzalutamide (Xtandi)</li> </ul> <p><b><u>Non-Step-Preferred:</u></b></p> <ul style="list-style-type: none"> <li>apalutamide (Erleada)</li> <li>darolutamide (Nubeqa) – Nov 2019</li> </ul>	<p>N/A – No <b>CYP-17 Inhibitors</b> or <b>2<sup>nd</sup>-Gen Antiandrogens</b> agents are designated non-formulary</p>
<p>*abiraterone acetate 250 mg (generic) no longer requires trial of Yonsa first – Nov 2019</p> <ul style="list-style-type: none"> <li>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</li> </ul> <p>apalutamide (Erleada) and darolutamide (Nubeqa) are UF, but non-step preferred</p> <ul style="list-style-type: none"> <li>must have a trial of enzalutamide (Xtandi) first</li> </ul> <p>Prior Authorization (PA) and Quantity Limits apply to all CYP-17 Inhibitors and 2<sup>nd</sup>-Gen Antiandrogens</p>		

# Drugs in Subclasses: CYP17 and 2<sup>nd</sup>-Gen AA



Generic/ Brand	MOA	FDA Approval Date	Dosage	Indication				Other
				nmHSPC	nmCRPC	mHSPC	mCRPC	GnRH*
abiraterone acetate (Zytiga)	Androgen Synthesis Inhibitor (CYP17)	Apr 2011	1000 mg once daily with prednisone	O	O	X	X	X
abiraterone acetate micronized (Yonsa)	Androgen Synthesis Inhibitor (CYP17)	May 2018	500 mg once daily with methylprednisolone	O	O	O	X	X
enzalutamide (Xtandi)	Androgen Receptor Inhibitor	Aug 2012	160 mg once daily		X	X	X	X
apalutamide (Erleada)	Androgen Receptor Inhibitor	Feb 2018	240 mg once daily		X	X		X
darolutamide (Nubeqa)	Androgen Receptor Inhibitor	Jul 2019	600 mg BID		X			X

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

\*GnRH = gonadotropin-releasing hormone (Patient must be receiving a GnRH analog concomitantly with all five drugs listed above OR have had a bilateral orchiectomy)

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

# Overall Clinical Conclusions (Feb 2019) for CYP17 and 2<sup>nd</sup>-Gen AA Agents



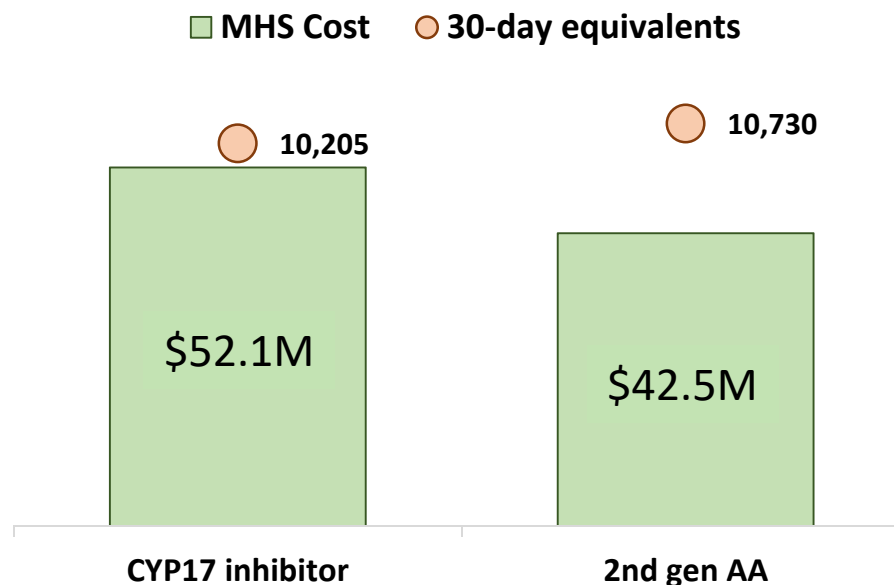
- Subclasses have two different mechanisms of action
- CYP17 subclass:
  - same molecular entity: abiraterone acetate
  - no difference in guideline driven recommendations between agents (both agents recommended in all non-localized forms of prostate cancer)
  - no clinically meaningful difference in safety between abiraterone agents; monitor patients for mineralocorticoid excess (BP, K<sup>+</sup>, and edema), adrenocortical insufficiency, and hepatotoxicity
- 2<sup>nd</sup>-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 nmCRPC 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 & 2<sup>nd</sup>-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

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# Selected Slides From February 2019 Cost Review



# Prostate Cancer agents Utilization and cost, one year



## CYP17 subclass

One Year	Number of 30DE	Net MHS Cost
Mail	4,600	\$20.7M
MTF	1,200	\$5.3M
Retail	4,400	\$26.1M
<b>Total</b>	<b>10,200</b>	<b>\$52.1M</b>

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

## 2<sup>nd</sup>-Gen AA subclass

One Year	30DE	Net MHS Cost
Mail	6,100	\$23.6M
MTF	1,400	\$6.1M
Retail	3,300	\$12.8M
<b>Total</b>	<b>10,800</b>	<b>\$42.5M</b>

apalutamide (Erleada)  
 enzalutamide (Xtandi)

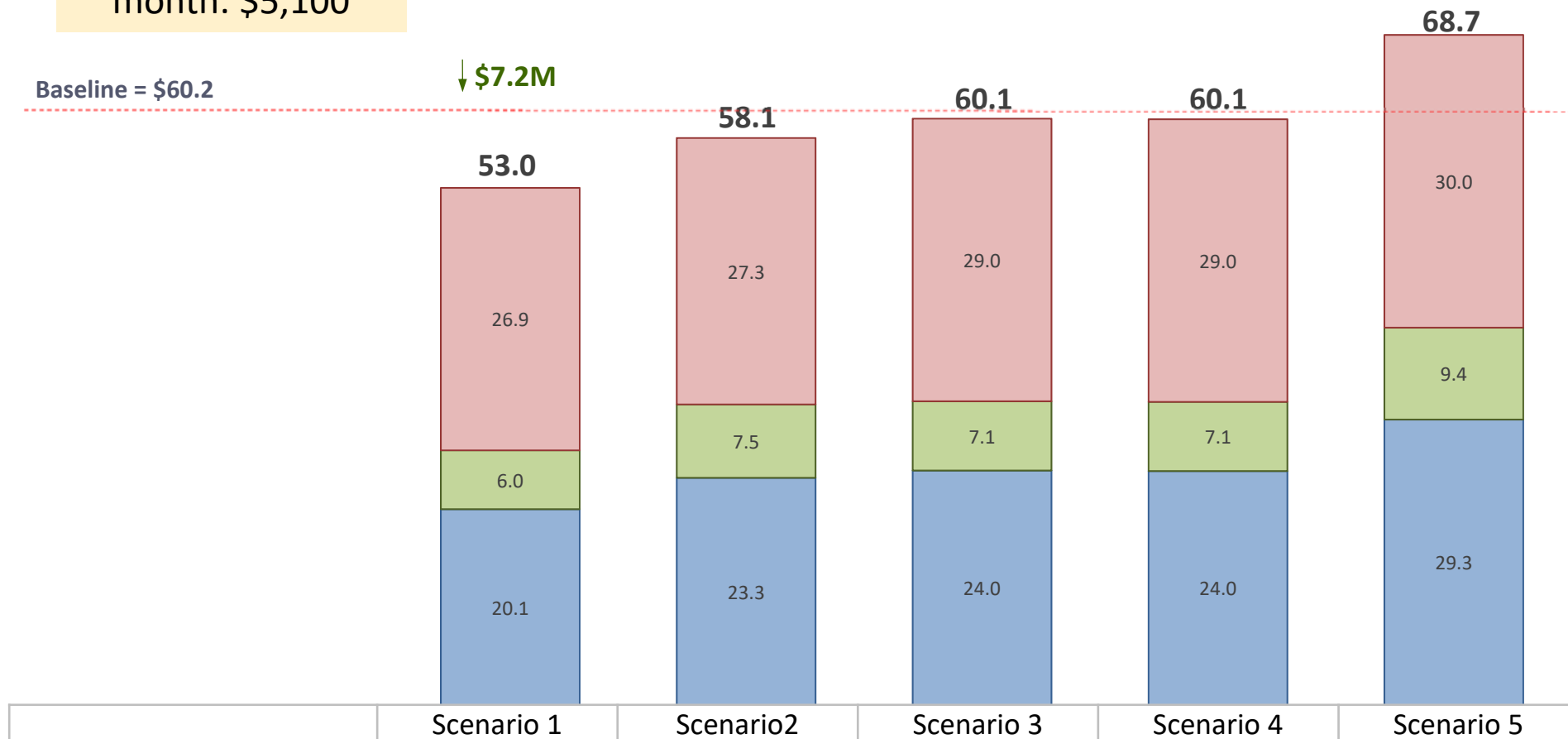
From Feb 2019 review

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



Average cost per month: \$5,100

Mail MTF Retail

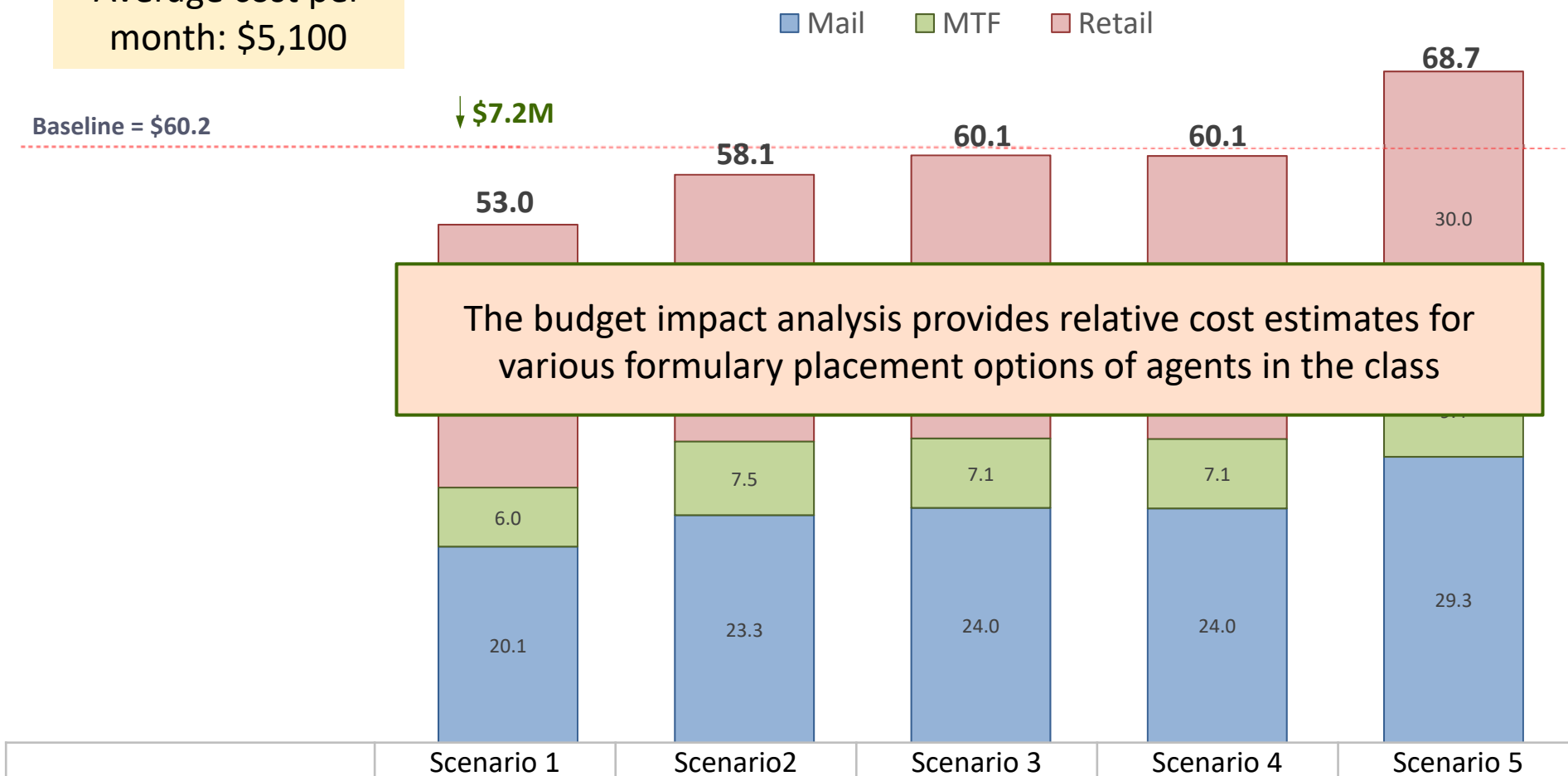


From Feb 2019 review

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



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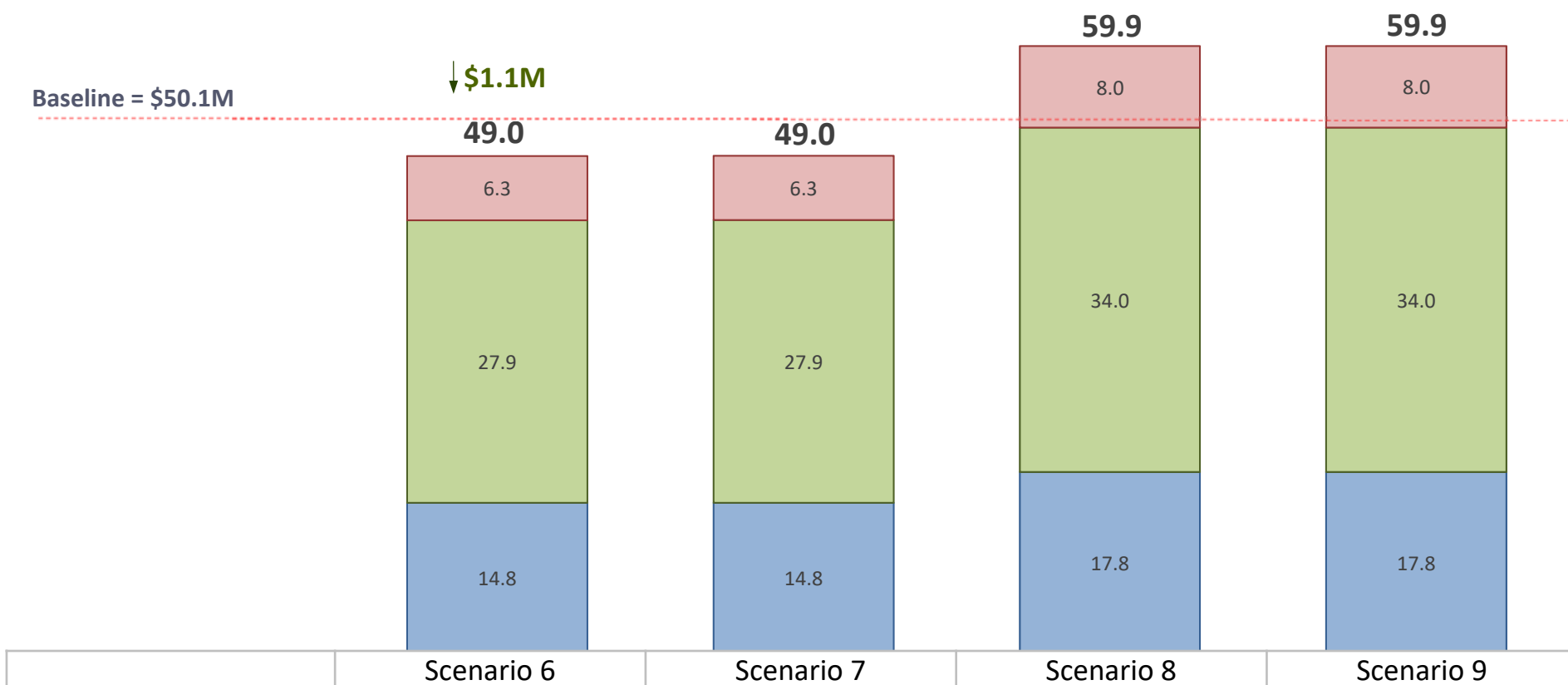
From Feb 2019 review

# Budget Impact Analysis – 2<sup>nd</sup>-Gen AA Outlook – One Year



Average cost per month: \$3,900

Mail MTF Retail



# Committee Recommendations

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- Formulary Status Recommendations:
  - Step-preferred/Tier 1: Yonsa (CYP17); Xtandi (2<sup>nd</sup> Gen AA)
  - UF/non-step-preferred: Zytiga (CYP17); Erleada (2<sup>nd</sup> Gen AA)
  
- CYP17: No grandfathering
- 2<sup>nd</sup> Gen AA: Grandfathered
  
- CYP17 prior authorization criteria required Yonsa step-preferred, then abiraterone 250mg before abiraterone 500mg

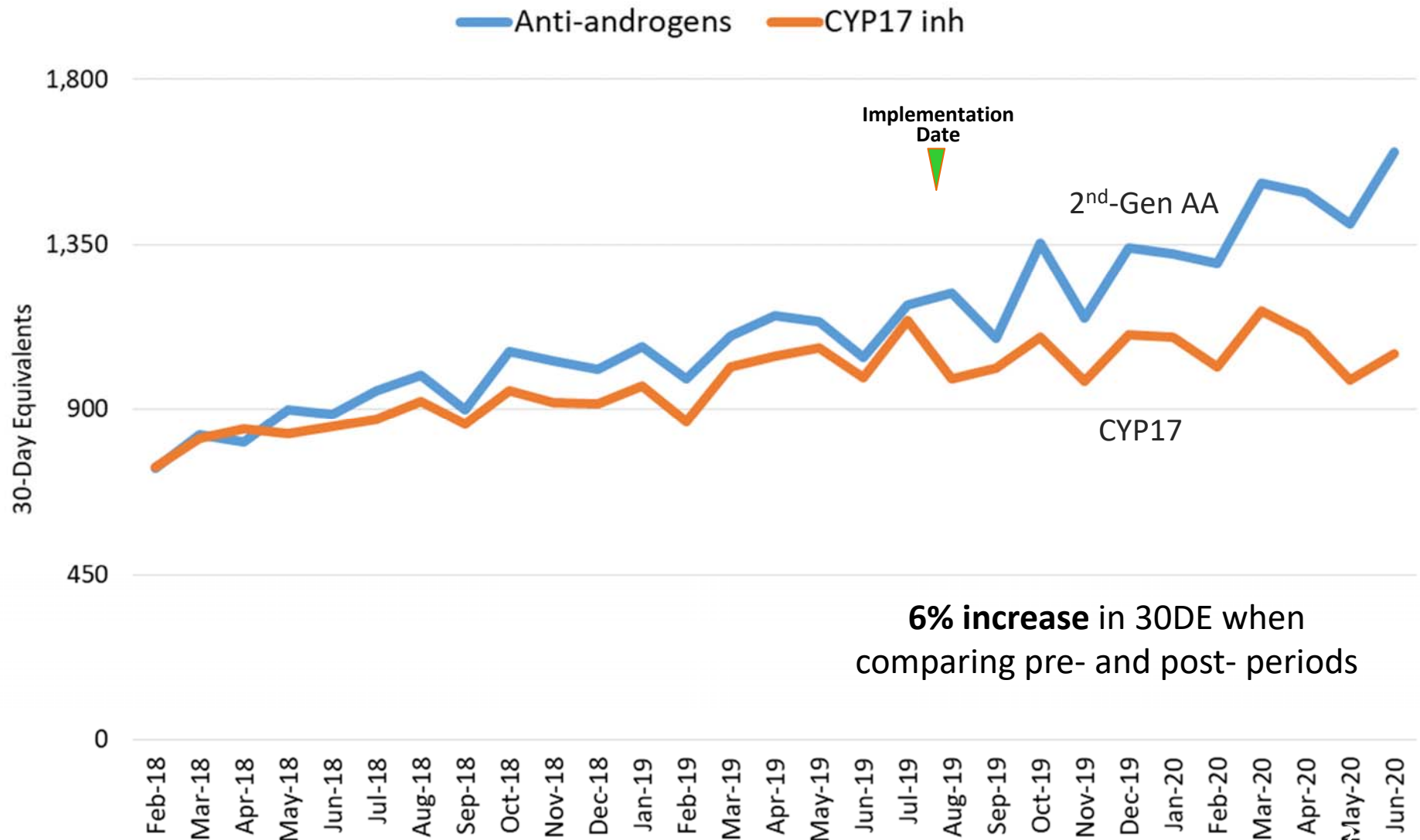
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# Post-implementation results

## Implemented Aug 2019

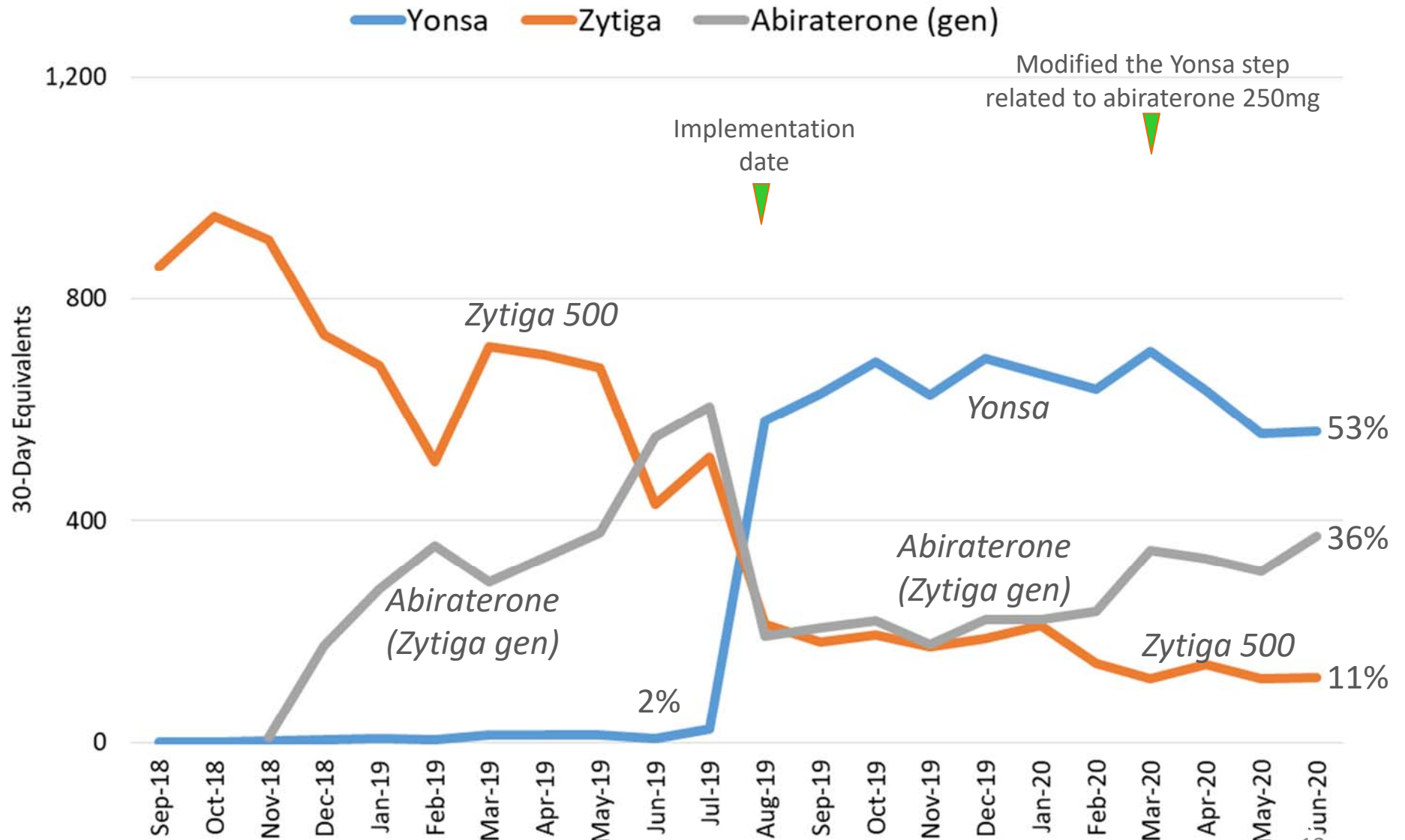
# Prostate Cancer Agents 30-Day Equivalents

**CYP17:** abiraterone (Zytiga) and abiraterone submic (Yonsa)  
**2<sup>nd</sup>-Gen AA:** apalutamide (Erleada) and enzalutamide (Xtandi)



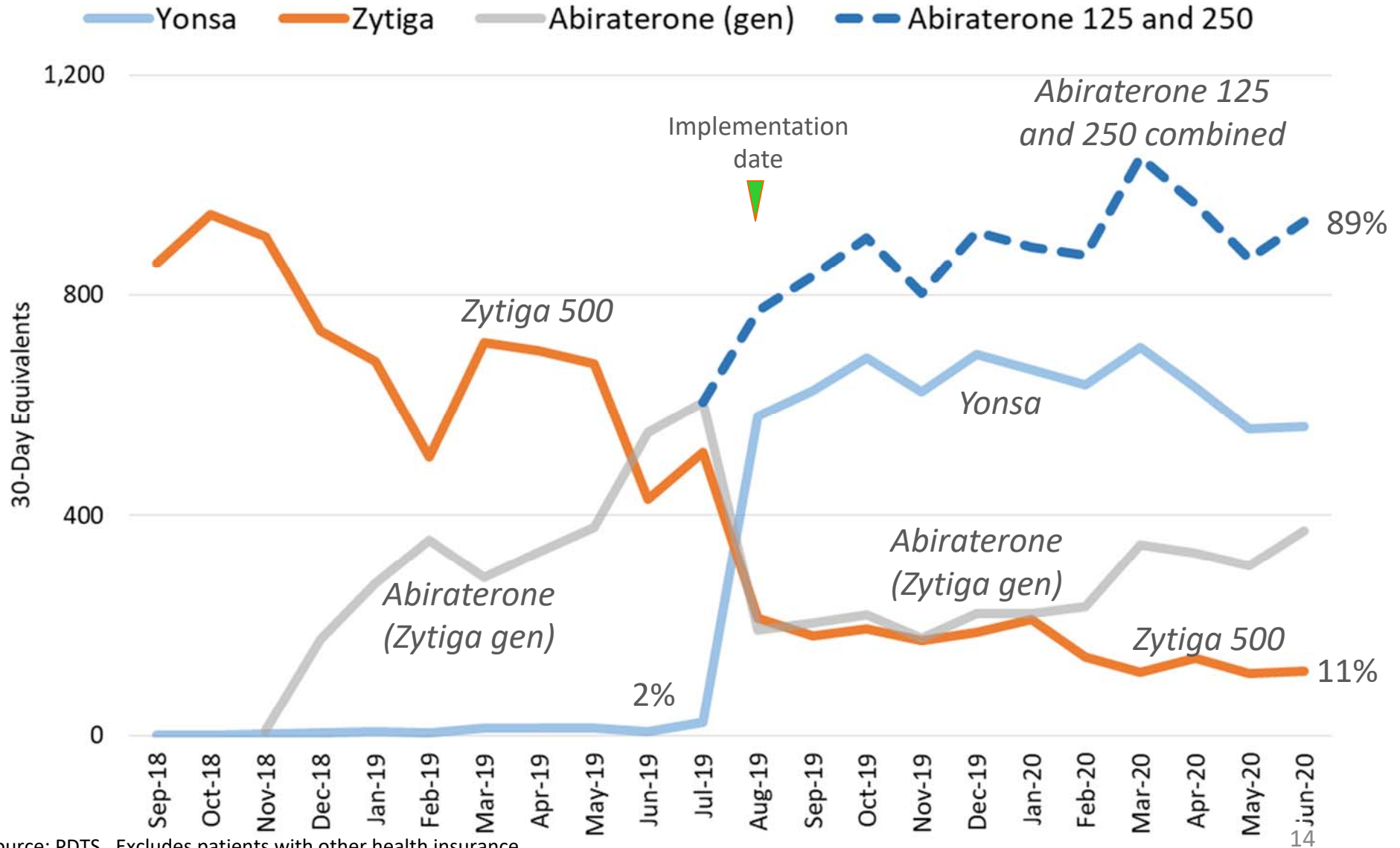
Source: PDTs. Excludes patients with other health insurance.

# CYP17 Subclass 30-Day Equivalents



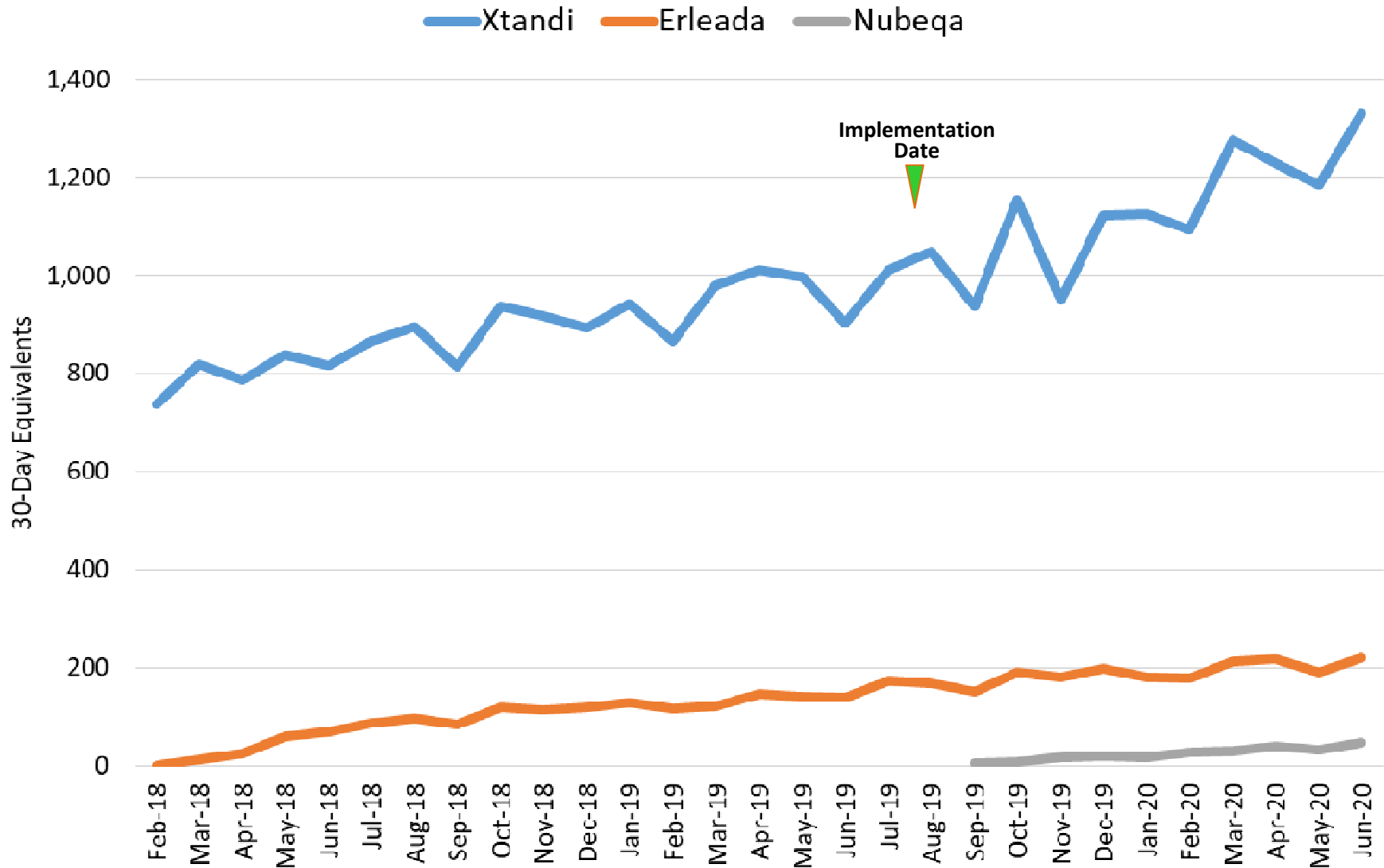
Source: PDTS. Excludes patients with other health insurance.

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Source: PDTS. Excludes patients with other health insurance.

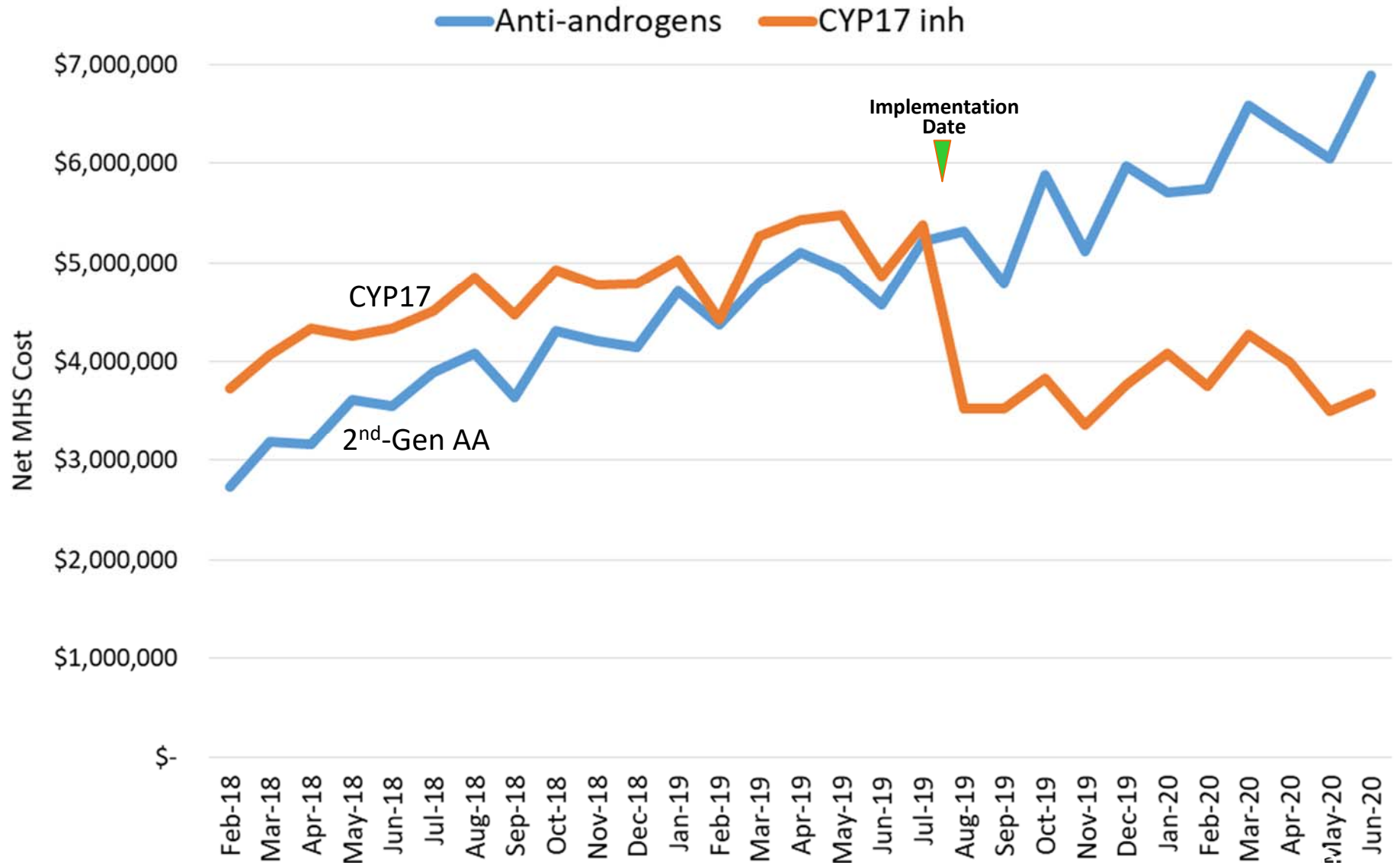
# 2<sup>nd</sup>-Gen AA Subclass 30-Day Equivalents



Source: PDTS. Excludes patients with other health insurance.

# Prostate Cancer Agents Net MHS Cost

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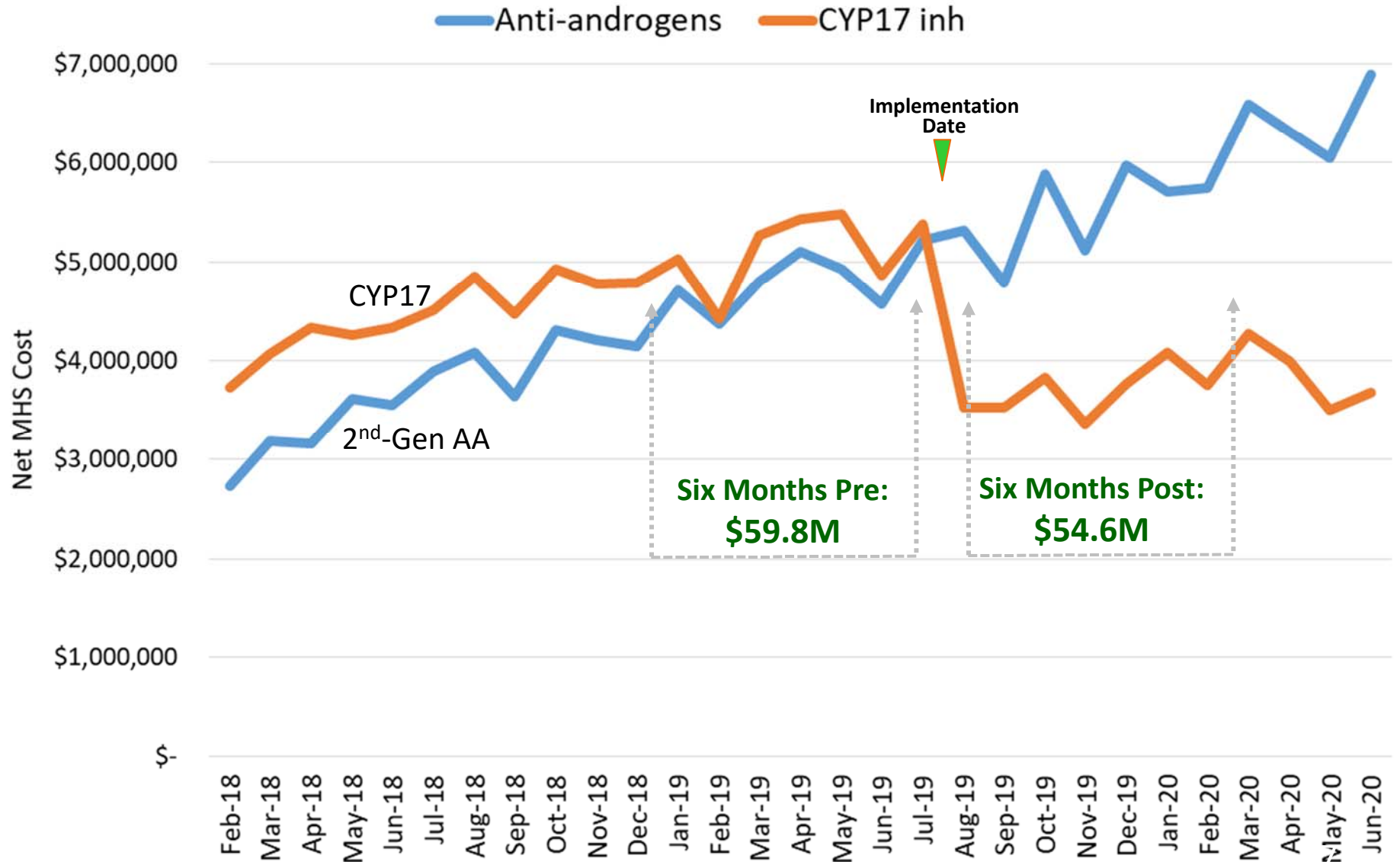


Source: PDTs. Excludes patients with other health insurance.



# Prostate Cancer Agents Net MHS Cost

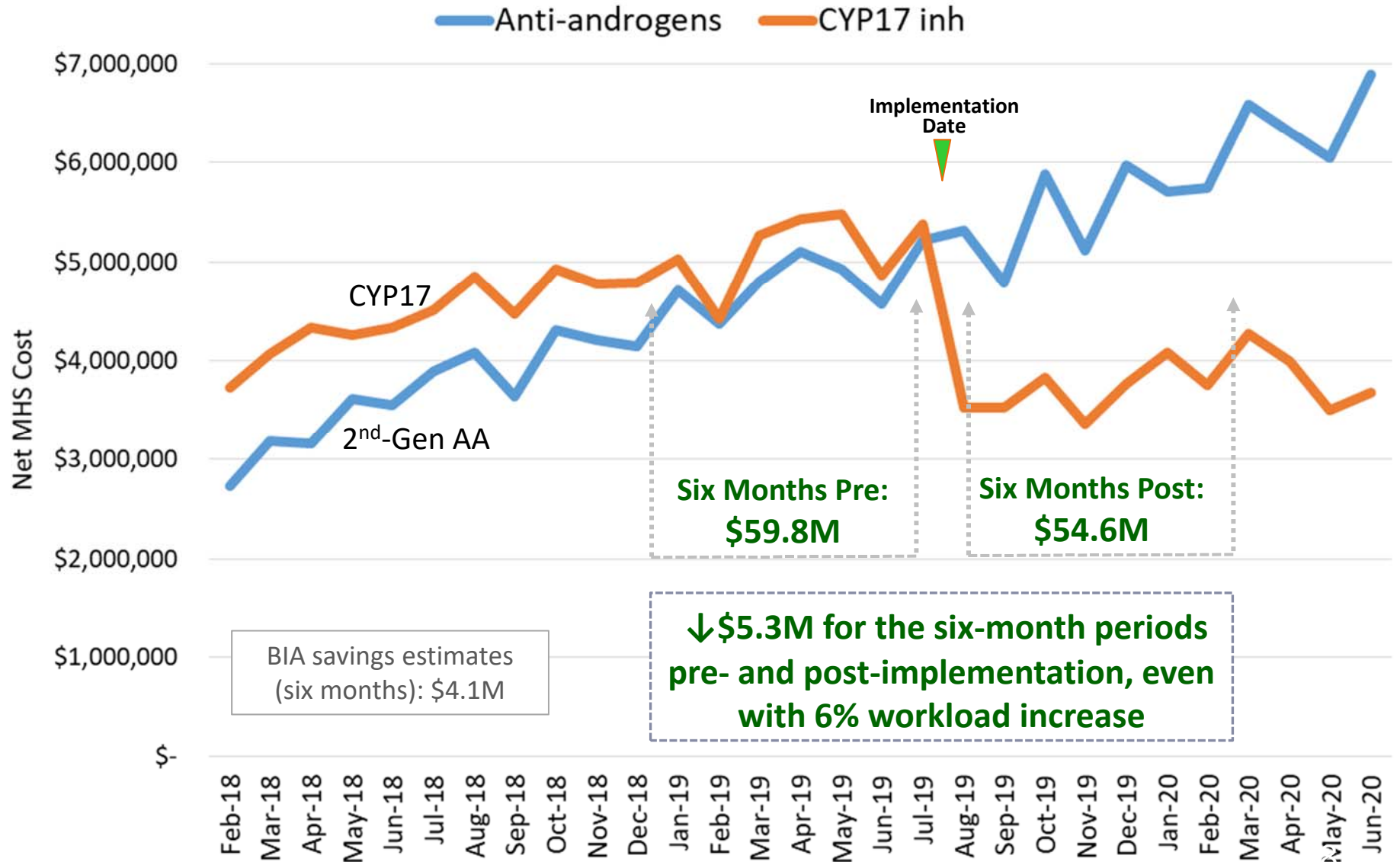
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Source: PDTs. Excludes patients with other health insurance

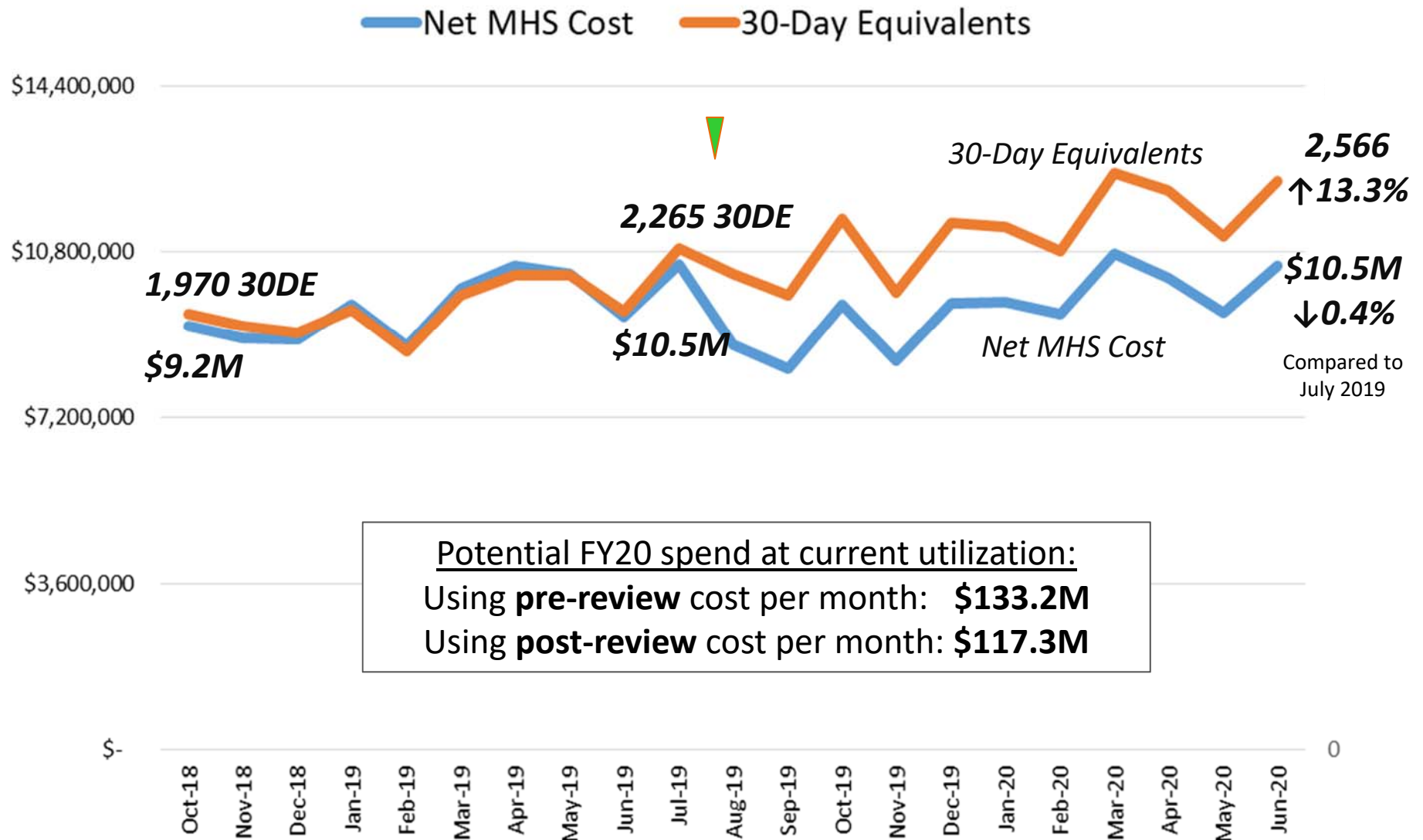
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Source: PDTs. Excludes patients with other health insurance

# Prostate Cancer Agents Summary of Cost and Workload (30DE)



# 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>
  - Formulary management tools can have a huge impact, everyone plays a role in successful implementation