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## 5.21.028

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2026
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	November 8, 2012
<b>Subject:</b>	Zytiga	<b>Page:</b>	1 of 7

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**Last Review Date:** December 12, 2025

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### Zytiga

#### Description

Zytiga (abiraterone acetate)

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#### Background

Zytiga (abiraterone acetate) is indicated to treat patients with prostate cancer. Zytiga targets a protein called cytochrome P450 17A1 (CYP17A1) which helps to prevent the conversion of androgens to testosterone and reduces the potential growth of prostate cancer cells (1).

#### Regulatory Status

FDA-approved indications: Zytiga is a CYP17 inhibitor indicated in combination with prednisone for the treatment of patients with: (1)

- Metastatic castration-resistant prostate cancer (CRPC)
- Metastatic high-risk castration-sensitive prostate cancer (CSPC)

Zytiga is indicated in combination with Lynparza and prednisone or prednisolone for the treatment of adult patients with deleterious or suspected deleterious *BRCA*-mutated (*BRCA*m) metastatic castration-resistant prostate cancer (mCRPC) (3).

#### Off-Label Use: (2)

- Very-high-risk non-metastatic prostate cancer

Zytiga may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Zytiga should be used with caution in patients with a history of cardiovascular disease. Before treatment is initiated, hypertension should be controlled, and hypokalemia should be corrected. Blood pressure,

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2026
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	November 8, 2012
<b>Subject:</b>	Zytiga	<b>Page:</b>	2 of 7

---

serum potassium, and symptoms of fluid retention should be monitored at least monthly. Adrenal cortical insufficiency may occur with the use of Zytiga. Adrenal insufficiency has occurred during Zytiga treatment. Caution should be used and monitor for symptoms and signs of adrenocortical insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions, or experience unusual stress (1).

Zytiga may cause hepatotoxicity. Increases in liver enzymes have led to drug interruption, dose modification and/or discontinuation. Serum transaminases (ALT and AST) and bilirubin levels should be measured prior to initiation of therapy, every two weeks for the first three months of treatment, and monthly thereafter. Elevations of AST, ALT, or bilirubin from the patient's baseline should prompt more frequent monitoring. If at any time, AST or ALT rise above five times the upper limit of normal (ULN), or the bilirubin rises above three times the ULN, Zytiga treatment should be interrupted, and liver function closely monitored (1).

Zytiga can cause fetal harm. Male patients with female partners of reproductive potential should be advised to use effective contraception during treatment and for 3 weeks after the last dose of Zytiga (1).

The safety and effectiveness of Zytiga in pediatric patients have not been established (1).

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#### **Related policies**

Akeega, Erleada, Nilandron, Nubeqa, Orgovyx, Yonsa, Xtandi

#### **Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Zytiga may be considered **medically necessary** if the conditions indicated below are met.

Zytiga may be considered **investigational** for all other indications.

### **Prior-Approval Requirements**

#### **Abiraterone only**

**Age** 18 years of age and older

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2026
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	November 8, 2012
<b>Subject:</b>	Zytiga	<b>Page:</b>	3 of 7

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## Diagnoses

Patients must have **ONE** of the following:

1. Metastatic castration-resistant prostate cancer (CRPC) with **ONE** of the following:
  - a. Used in combination with prednisone
  - b. Used in combination with Lynparza and either prednisone or prednisolone
2. Metastatic high-risk castration-sensitive prostate cancer (CSPC)
  - a. Used in combination with prednisone
3. Non-metastatic very-high-risk prostate cancer
  - a. Used in combination with prednisone or methylprednisolone

**AND ALL** of the following for **ALL** indications:

- a. **NO** dual therapy with another Prior Authorization (PA) androgen receptor inhibitor (see Appendix 1)
- b. Male patients with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zytiga and for 3 weeks after the final dose

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## Zytiga only

**Age** 18 years of age and older

## Diagnoses

Patients must have **ONE** of the following with provided documentation (e.g., medical records, laboratory reports):

1. Metastatic castration-resistant prostate cancer (CRPC) with **ONE** of the following:
  - a. Used in combination with prednisone
  - b. Used in combination with Lynparza and either prednisone or prednisolone
2. Metastatic high-risk castration-sensitive prostate cancer (CSPC)
  - a. Used in combination with prednisone
3. Non-metastatic very-high-risk prostate cancer
  - a. Used in combination with prednisone or methylprednisolone

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**Section:** Prescription Drugs      **Effective Date:** January 1, 2026  
**Subsection:** Antineoplastic Agents      **Original Policy Date:** November 8, 2012  
**Subject:** Zytiga      **Page:** 4 of 7

---

**AND ALL** of the following for **ALL** indications:

- a. **NO** dual therapy with another Prior Authorization (PA) androgen receptor inhibitor (see Appendix 1)
- b. Male patients with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zytiga and for 3 weeks after the final dose
- c. Patient **MUST** have tried the preferred product(s) (see Appendix 2) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

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## Prior – Approval Renewal Requirements

Same as above

### Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

#### Quantity

Strength	Quantity
250 mg	360 tablets per 90 days <b>OR</b>
500 mg	180 tablets per 90 days

Duration      12 months

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### Prior – Approval Renewal Limits

Same as above

### Rationale

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2026
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	November 8, 2012
<b>Subject:</b>	Zytiga	<b>Page:</b>	5 of 7

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## Summary

Zytiga is a CYP17 inhibitor indicated for use in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer as well as for the treatment of metastatic high-risk castration-sensitive prostate cancer. Zytiga is also used off-label to treat non-metastatic prostate cancer that is very-high-risk. Zytiga may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Zytiga can cause fetal harm. Male patients with female partners of reproductive potential should be advised to use effective contraception during treatment and for 3 weeks after the last dose of Zytiga. The safety and effectiveness of Zytiga in pediatric patients have not been established (1-2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Zytiga while maintaining optimal therapeutic outcomes.

## References

1. Zytiga [package insert]. Horsham, PA: Janssen Biotech, Inc; August 2021.
2. NCCN Clinical Practice Guidelines in Oncology® Prostate Cancer (Version 4.2024). National Comprehensive Cancer Network, Inc. May 2024. Accessed on November 3, 2025.
3. Lynparza [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2023.

## Policy History

Date	Action
October 2012	New addition to PA
December 2012	New FDA indication to be used before treatment with chemotherapy Deleted requirement for prior treatment with docetaxel Annual editorial review and update
March 2014	Annual editorial review and reference update
March 2015	Annual editorial review and reference update
June 2016	Annual editorial review and reference update Policy code changed from 5.04.28 to 5.21.28
March 2017	Annual review and reference update
February 2018	Addition of no dual therapy with another androgen receptor inhibitor Addition of the diagnosis of metastatic high-risk castration-sensitive prostate cancer (CSPC) to criteria Added Quantity Limits
June 2018	Annual editorial review
September 2018	Annual editorial review and reference update

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2026
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	November 8, 2012
<b>Subject:</b>	Zytiga	<b>Page:</b>	6 of 7

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June 2019	Annual review
December 2019	Annual review and reference update Addition of requirement to trial preferred product
June 2020	Annual review
March 2021	Annual editorial review and reference update Added requirement for the use of effective contraception for female partners of reproductive potential to align with package insert and related policies
June 2021	Annual review and reference update
June 2022	Addition of indication per reconsideration review and NCCN: non-metastatic very-high-risk prostate cancer
September 2022	Annual review and reference update
December 2022	Annual review and reference update
June 2023	Per Lynparza PI update, added "used in combination with Lynparza and either prednisone or prednisolone" as an option for mCRPC
September 2023	Annual review and reference update
December 2023	Annual review and reference update
March 2024	Annual review and reference update
December 2024	Annual review and reference update
December 2025	Annual editorial review and reference update. Added documentation requirement for brand Zytiga

## Keywords

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**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 12, 2025 and is effective on January 1, 2026.**

**Section:** Prescription Drugs      **Effective Date:** January 1, 2026  
**Subsection:** Antineoplastic Agents      **Original Policy Date:** November 8, 2012  
**Subject:** Zytiga      **Page:** 7 of 7

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## Appendix 1 - List of PA Androgen Receptor Inhibitors

Generic Name	Brand Name
abiraterone	Yonsa
abiraterone	Zytiga
abiraterone/niraparib	Akeega
apalutamide	Erleada
darolutamide	Nubeqa
enzalutamide	Xtandi
nilutamide	Nilandron

## Appendix 2 - List of Preferred Products

List of preferred products:

[https://info.caremark.com/content/dam/enterprise/caremark/microsites/dig/pdfs/pa-fep/fep-misc/FEP\\_ProductMedChx.pdf](https://info.caremark.com/content/dam/enterprise/caremark/microsites/dig/pdfs/pa-fep/fep-misc/FEP_ProductMedChx.pdf)

Refer to formulary documents for confirmation of coverage:

<https://www.fepblue.org/pharmacy/prescriptions#drug-lists>