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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Antineoplastic Agents	**Original Policy Date:**	November 8, 2012
Subject:	Zytiga	**Page:**	1 of 6

Last Review Date: March 12, 2021

Zytiga

Description

Zytiga (abiraterone acetate)

Background
Zytiga (abiraterone acetate) is indicated in combination with prednisone to treat men with late-stage (metastatic) castration-resistant prostate cancer, or prostate cancer that has spread to other parts of the body and is also resistant to medical or surgical treatments that lower testosterone. Zytiga is also indicated in combination with prednisone to treat men with metastatic high-risk castration-sensitive 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 indication: 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 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 corrected. Blood pressure, 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insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions, or experience unusual stress (1).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 and female patients have not been established (1).

Related policies
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** in male patients 18 years of age older for the treatment of metastatic castration resistant prostate cancer, or metastatic high-risk castration-sensitive prostate cancer and if the conditions indicated below are met.

Zytiga may be considered **investigational** in patients who are female, in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Gender Male

Diagnoses

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

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

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

a. Using in combination with prednisone
b. **NO** dual therapy with another androgen receptor inhibitor (see Appendix 1)
c. 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
d. **Brand Zytiga only:** Patient **MUST** have tried the preferred product (generic Zytiga: abiraterone acetate) unless the patient has a valid medical exception (e.g. inadequate treatment response, intolerance, contraindication)

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 **OR**
500 mg	180 tablets per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

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 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 and female patients have not been established (1).

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; October 2020.

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 Addition of no dual therapy with another androgen receptor inhibitor
February 2018	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
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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.

Appendix 1 - List of Androgen Receptor Inhibitors

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