ZYTIGA® (abiraterone acetate) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member’s specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

Description:

Zytiga (abiraterone) is a cytochrome P450 17 (CYP17, also known as 17 alpha-hydroxylase) inhibitor indicated in combination with Prednisone for the treatment of metastatic castration-resistant prostate cancer.

CYP17 catalyzes two consecutive reactions: 1) the conversion of pregnenolone and progesterone to their 17alpha hydroxy derivatives by 17 alpha-hydroxylase and 2) the subsequent formation of dehydroepiandrosterone (DHEA) and androstenedione, respectively, by C17, 20 lyase. DHEA and androstenedione are androgens and are precursors of testosterone. CYP17 enzyme is expressed in testicular, adrenal, and prostatic tumor tissues and is required for androgen biosynthesis. Androgen sensitive prostatic carcinoma responds to treatment that decreases androgen levels. Androgen deprivation therapies, such as treatment with gonadotropin-releasing hormone (GnRH) agonists or orchiectomy, decrease androgen production in the testes but do not affect androgen production by the adrenals or in the tumor. Zytiga (abiraterone) decreased serum testosterone and other androgens.
ZYTIGA® (abiraterone acetate) oral tablet (cont.)

Definitions:

Drug related events:

Ineffective / failure
Use of a drug employing optimal doses (FDA-recommended doses) for optimal duration; where the condition being treated has not improved or worsened

A request for branded agent due to generic drug failure or ineffectiveness will be assessed for potential approval with documentation of use of optimal dose / duration of the generic product and meeting other criteria within the coverage guideline. When the drug in question is a combination product, there must be documentation of failure / ineffectiveness of concurrent use (each ingredient used at the same time) of individual generic components. When the drug in question is a low dose formulation, there must be documentation of failure / ineffectiveness of low dose generic formulation.

Adverse Drug Event: Allergic reaction / Hypersensitivity / Intolerance
Use of a drug produced a significant reaction where continued use of the drug places the individual at risk for either lack of improvement or worsening of the condition being treated or at risk for harm and the concern is documented in medical record. A significant adverse drug event is when an individual’s outcome is death, life-threatening, hospitalization (initial or prolonged), disability resulting in a significant, persistent, or permanent change, impairment, damage or disruption in the individuals’ body function/structure, physical activities or quality of life, or requires intervention to prevent permanent impairment or damage.

Allergic reaction / hypersensitivity – may or may not involve the active ingredient. When the active ingredient is involved, use of same or a chemically similar agent places the individual at risk for harm when the same or chemically similar agent is used. The subsequent reaction may be the same as the original reaction or a more exaggerated response may be seen, potentially placing the individual at even greater risk for harm.

If the reaction occurred from the active/main generic ingredient; request for branded agent with same active ingredient will not be considered unless it is proven (documented) that active ingredient did not cause reaction and the request meets other criteria within the coverage guideline

Intolerance – these events represent circumstance(s) where use of a drug produced a significant reaction and continued use may result in non-adherence to proposed therapy and this concern is documented in medical record

Contraindication
Use of a drug that is not recommended by the manufacturer or FDA labelling

Use of any drug in the face of a contraindication is outside of the FDA and manufacturer’s labelled recommendation and is considered investigational or experimental

Non-adherence
Individual does not follow prescribe regimen that places the individual at risk for lack of improvement or worsening of the condition being treated and this concern is documented in medical record
ZYTIGA® (abiraterone acetate) oral tablet (cont.)

**Precertification:**

Precertification (Prior Authorization) is required for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) pharmacy benefit for medication(s) or product(s) indicated in this guideline.

This Pharmacy Coverage Guideline does not apply to FEP or other states’ Blues Plans.

Information about medications that require precertification is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy).

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

**Criteria:**

See “Resources” section for FDA-approved dosage.

- Precertification for Zytiga (abiraterone acetate) oral tablet requires completion of the specific request form in its entirety. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com). Incomplete forms will be returned.

- FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Zytiga (abiraterone acetate) is considered *medically necessary* when ALL of the following criteria are met:

  1. Individual is male and 18 years of age or older
  2. Individual has medical record documentation of a confirmed diagnosis of metastatic castration-resistant prostate cancer, to be used in combination with Prednisone
  3. **ALL** of the following baseline tests have been completed before initiation of treatment:
     - Comprehensive metabolic panel
     - Blood pressure
     - Complete blood count
     - Lipid profile
  4. Absence of **ALL** of the following exclusions:
     - Individual with LVEF < 50% or NYHA Class II or NYHA Class III or IV heart failure
     - Individual with baseline severe hepatic impairment (Child-Pugh Class C)
     - In individuals with baseline moderate hepatic impairment who experienced ALT and AST elevations greater than 5 times the upper limit of normal while on Zytiga
     - In individuals with baseline moderate hepatic impairment who experienced total bilirubin greater than 3 times the upper limit of normal while on Zytiga
ZYTIGA® (abiraterone acetate) oral tablet (cont.)

- In individuals who develop hepatotoxicity while on Zytiga therapy and who continue to have hepatotoxicity with retreatment at the lowest dose of 500 mg once daily
- In individuals who experience a concurrent ALT elevation greater than 3 times the upper limit of normal and a total bilirubin greater than 2 times the upper limit of normal in the absence of biliary obstruction or other cause for the elevations
- Male using Zytiga who has a female partner of child bearing age and is not using a condom and another form of contraception
- Woman of child bearing age who is pregnant who has a male partner on Zytiga and is not using a condom

OR

- A non-FDA approved use for the treatment of cancer of Zytiga (abiraterone acetate) is considered medically necessary when ONE of the following criteria are met:

1. A non-FDA approved use for the treatment of cancer is recognized as safe and effective for the requested type of cancer, that is listed and supported by in ONE of the nationally recognized compendia or guidelines:
   - American Hospital Formulary Service
   - National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium
   - Thomson Micromedex compendium DrugDex
   - Elsevier Gold Standard’s Clinical Pharmacology compendium
   - American Society of Clinical Oncologist (ASCO) treatment guidelines
   - Other authoritative reference as identified by the Secretary of the United States Department of Human Health Services

2. A non-FDA approved use for the treatment of cancer that is established from clinical trial(s) that have been published in peer reviewed professional medical journal(s) that has been submitted by the prescriber if ALL of the following apply:
   - At least two articles from major peer reviewed professional medical journals have recognized, based on scientific or medical criteria, the drug's safety and effectiveness for treatment of the indication for which the drug has been prescribed
   - No article from a major peer reviewed professional medical journal has concluded, based on scientific or medical criteria, that the drug is unsafe or ineffective or that the drug’s safety and effectiveness cannot be determined for the treatment of the indication for which the drug has been prescribed
   - The literature meets the uniform requirements for manuscripts submitted to biomedical journals established by the international committee of medical journal editors or is published in a journal specified by the United States department of health and human services as acceptable peer reviewed medical literature pursuant to section 186(t)(2)(B) of the social security act (42 United States Code section 1395x(t)(2)(B))

- Oncology medications for all other indications not previously listed is considered experimental or investigational based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
3. Insufficient evidence to support improvement of the net health outcome, and
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
5. Insufficient evidence to support improvement outside the investigational setting.

This includes but is not limited to the following:
- Use in women

Resources:

FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZYTIGA is a CYP17 inhibitor indicated in combination with prednisone for</td>
<td>ZYTIGA 1,000 mg (four 250 mg tablets) administered orally once daily in combination with prednisone 5 mg administered orally twice daily. ZYTIGA must be taken on an empty stomach. No food should be consumed for at least two hours before the dose of ZYTIGA is taken and for at least one hour after the dose of ZYTIGA is taken. The tablets should be swallowed whole with water. Do not crush or chew tablets.</td>
</tr>
<tr>
<td>the treatment of patients with metastatic castration-resistant prostate</td>
<td></td>
</tr>
<tr>
<td>cancer.</td>
<td></td>
</tr>
</tbody>
</table>

- For patients with baseline moderate hepatic impairment (Child-Pugh Class B), reduce the ZYTIGA starting dose to 250 mg once daily.

- For patients who develop hepatotoxicity during treatment, hold ZYTIGA until recovery. Retreatment may be initiated at a reduced dose. ZYTIGA should be discontinued if patients develop severe hepatotoxicity.