Clinical Policy: Abiraterone (Zytiga)

Reference Number: CP.PHAR.84
Effective Date: 10/11
Last Review Date: 10/16 Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for abiraterone (Zytiga®) tablets for oral use.

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Zytiga is **medically necessary** when one of the following criteria are met:

I. Initial Approval Criteria

A. Prostate Cancer (must meet all)**:**

1. Diagnosis of metastatic castration-resistant prostate cancer (CRPC);
2. Zytiga will be used in combination with prednisone;
3. Prescribed dose of Zytiga does not exceed 1,000 mg per day (1,000 mg twice per day if concomitant use with a strong CYP3A4 inducer [e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, phenobarbital]);
4. Member does not have severe hepatic impairment (Child-Pugh Class C).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Prostate Cancer (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Prescribed dose of Zytiga does not exceed 1,000 mg per day (1,000 mg twice per day if concomitant use with a strong CYP3A4 inducer [e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, phenobarbital]);
3. Member has none of the following reasons to discontinue:
   a. Disease progression or unacceptable toxicity;
   b. In patients with moderate hepatic impairment: elevations in alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) greater than 5X upper limit of normal (ULN) or total bilirubin greater than 3X ULN;
   c. Hepatotoxicity at a dose of 500 mg once daily;
   d. Development of concurrent elevation of ALT greater than 3 x ULN and total bilirubin greater than 2 X ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation;
   e. Severe hepatic impairment (Child Pugh Class C).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Zytiga is a 17 α‑hydroxylase/C17,20-lyase (CYP17) inhibitor. Abiraterone acetate (Zytiga) is converted *in vivo* to abiraterone, an androgen biosynthesis inhibitor that inhibits CYP17. This enzyme is expressed in testicular, adrenal, and prostatic tumor tissues and is required for androgen biosynthesis. CYP17 catalyzes two sequential reactions: 1) the conversion of pregnenolone and progesterone to their 17α-hydroxy derivatives by 17α-hydroxylase activity and 2) the subsequent formation of dehydroepiandrosterone (DHEA) and androstenedione, respectively, by C17, 20 lyase activity. DHEA and androstenedione are androgens and are precursors of testosterone. Inhibition of CYP17 by abiraterone can also result in increased mineralocorticoid production by the adrenals.

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.

Formulations:

Zytiga is available in 250 mg tablets for oral administration.

FDA Approved Indications:

Zytiga is a CYP17 inhibitor/oral tablet formulation indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.

Appendices

Appendix A: Abbreviation Key

ALT: alanine aminotransferase
AST: aspartate aminotransferase
CRPC: castration-resistant prostate cancer
CYP17: 17 α‑hydroxylase/C17,20-lyase
DHEA: dehydroepiandrosterone
GnRH: gonadotropin-releasing hormone
ULN: upper limit of normal

Reviews, Revisions, and Approvals	Date	Approval Date
No clinical changes	11/12	12/12
Added hepatic impairment dosing to algorithm and Safety section Removed requirement for prior chemo treatment to algorithm	12/13	01/14
Updated background information Removed dose verification for hepatic toxicity from algorithm	12/14	12/14

Reviews, Revisions, and Approvals	Date	Approval Date
Converted policy to bullet format Limited references to PI (updated) and NCCN guidelines (updated); edited narrative accordingly Added abbreviation key, safety appendix; deleted appendix about disease progression (criteria not clearly defined in guidelines) Deleted dose adjustment table and instructions on how to take Zytiga with food In criteria section, eliminated documentation requests, added age requirement, added question about Zytiga contraindications per PI, kept disease progression question but deleted reference to appendix, removed question about whether would be used with additional treatment, added initial approval period of 3 months and kept 6 months for continuation approval period	09/15	11/15
Policy converted to new template. Removed age and prescriber specialty requirements. Added max dose requirement. Updated reasons to discontinue. Approval duration changed to 6 months for initial and 12 months for renewal.	10/16	11/16
Added max dose for concomitant use with a strong CYP3A4 inducer.	1/17	

References

1. Zytiga Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; May 2016. Available at: https://www.zytiga.com/. Accessed August 9, 2016.
2. Abiraterone acetate. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed August 10, 2016.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.