Clinical Policy: Abiraterone (Zytiga, Yonsa)

Reference Number: CP.PHAR.84
Effective Date: 10.01.11
Last Review Date: 02.20
Line of Business: Commercial, HIM, Medicaid

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

Description
Abiraterone (Zytiga®, Yonsa®) is a selective and irreversible inhibitor of enzyme CYP17.

FDA Approved Indication(s)
Zytiga is indicated in combination with prednisone for the treatment of metastatic castration-resistant prostate cancer and metastatic high-risk castration-sensitive prostate cancer.

Yonsa is indicated in combination with methylprednisolone for the treatment of patients with metastatic castration-resistant prostate cancer.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Zytiga and Yonsa are medically necessary when the following criteria are met:

I. Initial Approval Criteria

   A. Prostate Cancer (must meet all):
      1. Diagnosis of metastatic prostate cancer;
      2. Prescribed by or in consultation with an oncologist or urologist;
      3. Age ≥ 18 years;
      4. Member will use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy;
      5. For Zytiga requests: prescribed in combination with prednisone;
      6. For Yonsa requests: prescribed in combination with methylprednisolone;
      7. For Brand Zytiga and Yonsa requests: Medical justification supports inability to use generic abiraterone (e.g., contraindications to the excipients);
      8. Request meets one of the following (a, b, or c):*
         a. Zytiga: Dose does not exceed 1,000 mg once daily, or 1,000 mg twice daily if prescribed concomitantly with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, and phenobarbital);
         b. Yonsa: Dose does not exceed 500 mg per day, or 500 mg twice daily if prescribed concomitantly with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, and phenobarbital);
         c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
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*Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

B. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
A. Prostate Cancer (must meet all):
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Zytiga or Yonsa for metastatic prostate cancer and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Brand Zytiga and Yonsa requests: Medical justification supports inability to use generic abiraterone (e.g., contraindications to the excipients);
4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. Zytiga: New dose does not exceed 1,000 mg once daily, or 1,000 mg twice daily if prescribed concomitantly with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, and phenobarbital);
   b. Yonsa: New dose does not exceed 500 mg per day, or 500 mg twice daily if prescribed concomitantly with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, and phenobarbital);
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration:
Medicaid/HIM – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.
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IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

- ADT: androgen deprivation therapy
- CRPC: castration-resistant prostate cancer
- CSPC: castration-sensitive prostate cancer
- CYP17: cytochrome 17 α-hydroxylase/C17,20-lyase
- FDA: Food and Drug Administration
- LHRH: luteinizing hormone-releasing hormone

Appendix B: Therapeutic Alternatives

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>abiraterone (Zytiga®)</td>
<td>1,000 mg (four 250 mg tablets) PO QD in combination with prednisone 5 mg PO BID (CRPC) or prednisone 5 mg PO QD (CSPC)</td>
<td>1,000 mg QD; 1,000 mg BID if taking a strong CYP3A4 inducer</td>
</tr>
</tbody>
</table>

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): pregnancy (Yonsa only)
- Boxed warning(s): none reported

Appendix D: General Information

- Castration-resistant prostate cancer is prostate cancer that progresses clinically, radiographically, or biochemically despite castrate levels of serum testosterone (< 50 ng/dL). Per the NCCN, androgen deprivation therapy (ADT) should be continued in the setting of CRPC while additional therapies are applied.

- Examples of ADT include:
  - Bilateral orchiectomy (surgical castration)
  - Luteinizing hormone-releasing hormone (LHRH) given with or without an anti-androgen:
    - LHRH agonists: Zoladex® (goserelin), Vantas® (histrelin), leuprolide (Lupron Depot®, Eligard®), and Trelstar® (tiotrexetin)
    - Anti-androgens: bicalutamide (Casodex®), flutamide, nilutamide (Nilandron®), Xtandi® (enzalutamide), Erleada® (apalutamide)
  - LHRH antagonist: Firmagon® (degarelix)

- Per the NCCN prostate cancer guidelines version 4.2019:
  - For castration-naïve metastatic (M1) prostate cancer: Zytiga + prednisone + ADT has a category 1 recommendation, while Yonsa + methylprednisolone + ADT has a category 2B recommendation.
  - For castration-resistant metastatic (M1) prostate cancer without visceral metastases: Zytiga + prednisone + ADT has a category 1 recommendation, while Yonsa + methylprednisolone + ADT has a category 2A recommendation.
  - For castration-resistant metastatic (M1) prostate cancer with visceral metastases: Both Zytiga + prednisone + ADT and Yonsa + methylprednisolone + ADT have category 2A recommendations.
V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen*</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abiraterone</td>
<td>Castration-resistant prostate cancer</td>
<td>1,000 mg (four 250 mg tablets or two 500 mg tablets) PO QD in combination with prednisone 5 mg PO BID</td>
<td>1,000 mg QD; 1,000 mg BID if taking a strong CYP3A4 inducer</td>
</tr>
<tr>
<td>(Zytiga)</td>
<td>Castration-naïve prostate cancer</td>
<td>1,000 mg (four 250 mg tablets or two 500 mg tablets) PO QD in combination with prednisone 5 mg PO QD</td>
<td>1,000 mg QD; 1,000 mg BID if taking a strong CYP3A4 inducer</td>
</tr>
<tr>
<td></td>
<td>Castration-resistant prostate cancer</td>
<td>500 mg (four 125 mg tablets) PO QD in combination with methylprednisolone 4 mg PO BID</td>
<td>500 mg QD; 500 mg BID if taking a strong CYP3A4 inducer</td>
</tr>
<tr>
<td></td>
<td>Castration-naïve prostate cancer</td>
<td></td>
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</tr>
</tbody>
</table>

*Patients receiving Zytiga or Yonsa should also receive a GnRH analog concurrently or should have had bilateral orchiectomy.

VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abiraterone</td>
<td>Film-coated tablet: 500 mg Uncoated tablet: 250 mg (generic available as coated and uncoated)</td>
</tr>
<tr>
<td>(Zytiga)</td>
<td></td>
</tr>
<tr>
<td>Abiraterone</td>
<td>Tablet: 125 mg</td>
</tr>
<tr>
<td>(Yonsa)</td>
<td></td>
</tr>
</tbody>
</table>

VII. References


Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>09.15</td>
<td>11.15</td>
</tr>
</tbody>
</table>
### Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td>10.16</td>
</tr>
<tr>
<td>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.</td>
<td>01.17</td>
</tr>
<tr>
<td>Added max dose for concomitant use with a strong CYP3A4 inducer.</td>
<td>09.17</td>
</tr>
<tr>
<td>Converted to new template. Initial: clarified CRPC. Re-auth: added clarification that Zytiga must be used in combination with; added efficacy requirement of positive response. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs.</td>
<td>03.06.18</td>
</tr>
<tr>
<td>Criteria added for new FDA indication: castration-sensitive prostate cancer.</td>
<td>05.15.18</td>
</tr>
<tr>
<td>3Q 2018 annual review: added HIM line of business; no significant changes from previously approved corporate policy; references reviewed and updated.</td>
<td>02.01.19</td>
</tr>
<tr>
<td>Changes align with previously approved clinical guidance: Added Yonsa to criteria requiring redirection to generic Zytiga per SDC.</td>
<td>02.01.19</td>
</tr>
<tr>
<td>2Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>03.06.19</td>
</tr>
<tr>
<td>1Q 2020 annual review: modified to require that a GnRH analog should always be prescribed concurrently with abiraterone unless member has had a bilateral orchietomy (regardless of CRPC or CSPC) per FDA labeling and NCCN guidelines; references reviewed and updated.</td>
<td>10.07.19</td>
</tr>
<tr>
<td>Added criterion for medical justification supporting inability to use generic abiraterone for brand Zytiga request.</td>
<td>07.23.20</td>
</tr>
</tbody>
</table>

### 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.