Clinical Policy: Enzalutamide (Xtandi)

Reference Number: CP.CPA.203
Effective Date: 11.16.16
Last Review Date: 02.20
Line of Business: Commercial

Revision Log

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

Description

Enzalutamide (Xtandi®) is an androgen receptor inhibitor.

FDA Approved Indication(s)

Xtandi is indicated for the treatment of patients with:

- Castration-resistant prostate cancer (CRPC)
- Metastatic castration-sensitive prostate cancer (CSPC)

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 Xtandi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of one of the following (a or b):
   a. CRPC, as evidenced by disease progression despite bilateral orchiectomy or other androgen deprivation therapy (*see Appendix D*);
   b. Metastatic CSPC;
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age ≥ 18 years;
4. For members with metastatic CRPC without visceral metastases or metastatic CSPC: Failure of Zytiga®, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for Zytiga*
5. Member will use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy;
6. Request meets one of the following (a, b, c, or d):*
   a. If prescribed concomitantly with a strong CYP2C8 inhibitor (e.g., gemfibrozil): Dose does not exceed 80 mg (2 capsules) per day;
   b. Dose does not exceed 160 mg (4 capsules) per day;
   c. If prescribed concomitantly with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, and phenobarbital): Dose does not exceed 240 mg (6 capsules) per day;

d. 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: 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.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Xtandi for prostate cancer and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, c, or d):*
   a. If prescribed concomitantly with a strong CYP2C8 inhibitor (e.g., gemfibrozil): New dose does not exceed 80 mg (2 capsules) per day;
   b. New dose does not exceed 160 mg (4 capsules) per day;
   c. If prescribed concomitantly with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, and phenobarbital): New dose does not exceed 240 mg (6 capsules) per day;
   d. 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: 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.

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.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ADT: androgen deprivation therapy
CRPC: castration resistant prostate cancer
CSPC: castration-sensitive prostate cancer
FDA: Food and Drug Administration
GnRH: gonadotropin-releasing hormone
LHRH: luteinizing hormone-releasing hormone

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Zytiga® (abiraterone)	1,000 mg PO QD (given in combination with prednisone)	1,000 mg/day; 2,000 mg/day if taking a strong CYP3A4 inducer

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
None reported

Appendix D: General Information
- CRPC 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® (triptorelin)
    - Anti-androgens: bicalutamide (Casodex®), flutamide, nilutamide (Nilandron®), Xtandi® (enzalutamide), Erleada® (apalutamide)
  - LHRH antagonist: Firmagon® (degarelix)
- NCCN guidelines on treatment of prostate cancer (version 4.2019):
  - In patients with metastatic castration-recurrent prostate cancer without visceral metastases, docetaxel, Zytiga with prednisone, Yonsa with methylprednisolone, or Xtandi are recommended as the first-line chemotherapy treatment for men with met (category 1 recommendation for all except Yonsa, which is 2A).
  - In patients with metastatic castrate-resistant prostate cancer who have visceral metastases, Xtandi or docetaxel have category 1 recommendations while Zytiga + prednisone and Yonsa + methylprednisolone have a category 2A recommendation. Visceral metastases refers to liver, lung, adrenal, peritoneal, and brain metastases. Soft tissue/lymph node sites are not considered visceral metastases.
  - In patients with metastatic CSPC, both Zytiga and Xtandi have category 1 recommendations.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CRPC, metastatic CSPC	160 mg (four 40 mg capsules) PO QD. Patients receiving Xtandi should also receive a GnRH analog concurrently or should have had bilateral orchiectomy	160 mg/day; 240 mg/day if taking a strong CYP3A4 inducer

VI. Product Availability

Capsule: 40 mg

VII. References

1. Xtandi Prescribing Information. Northbrook, IL: Astellas Pharma US, Inc.; December 2019. Available at: https://www.xtandi.com. Accessed December 17, 2019.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. December 17, 2019.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com/. Accessed December 17, 2019.
4. Enzalutamide. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed December 19, 2019.
5. National Comprehensive Cancer Network. Prostate Cancer Version 4.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed December 19, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Added NCCN Compendium supported use for castration naïve disease in combo with LHRH agonist.	05.30.17	11.17
3Q 2018 annual review: specialist requirement was added; off-label use in castration-naïve prostate cancer removed per NCCN guidelines; references reviewed and updated.	05.15.18	08.18
Criteria added for new FDA indication: non-metastatic CRPC; removed requirement for metastatic disease as Xtandi is now approved for non-metastatic prostate cancer; added requirement for non-metastatic disease that Xtandi be used with a GnRH analog or member has had a bilateral orchiectomy; clarified Zytiga redirection only applies to metastatic disease without visceral metastasis; added urologist prescriber option; references reviewed and updated.	08.28.18	02.19
2Q 2019 annual review: no significant changes; references reviewed and updated.	03.05.19	05.19
1Q 2020 annual review: criteria added for new FDA indication: metastatic CSPC; modified to require that a GnRH analog should always be prescribed concurrently with Xtandi unless member has had a bilateral orchiectomy (regardless of metastatic or non-metastatic disease) per FDA labeling and NCCN guidelines; clarified Zytiga redirection also applies to metastatic CSPC; references reviewed and updated.	01.14.20	02.20

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.

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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.

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