

Clinical Policy: Enzalutamide (Xtandi)

Reference Number: CP.CPA.203

Effective Date: 11.16.16

Last Review Date: 02.19

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).

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 CRPC, as evidenced by disease progression despite bilateral orchiectomy or other androgen deprivation therapy (*see Appendix D*);
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age \geq 18 years;
4. For members with metastatic disease without visceral metastases: failure of Zytiga® unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization is required for Zytiga*
5. For non-metastatic disease, member will use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy;
6. Dose does not exceed 160 mg per day (4 capsules per day), or 240 mg per day (6 capsules per day) if prescribed concomitantly with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, and phenobarbital).

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 CRPC 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, new dose does not exceed 160 mg per day (4 capsules per day), or 240 mg per day (6 capsules per day) if prescribed concomitantly with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, and phenobarbital).

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

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

- 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 3.2018) recommend docetaxel, Zytiga with prednisone, or Xtandi as the first-line chemotherapy treatment for men with metastatic castration-recurrent prostate cancer without visceral metastases (category 1 recommendation).
- In patients with metastatic castrate-resistant prostate cancer who have visceral metastases, Xtandi or docetaxel have category 1 recommendations while Zytiga + prednisone has a category 2A recommendation.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CRPC	160 mg (four 40 mg capsules) PO QD	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.; July 2018. Available at: <https://www.xtandi.com>. Accessed July 17, 2018.
2. Micromedex[®] Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. May 15, 2018.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: <http://www.clinicalpharmacology-ip.com/>.
4. Enzalutamide. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed July 17, 2018.
5. National Comprehensive Cancer Network. Prostate Cancer Version 02.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed July 17, 2018.

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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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

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.

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recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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