Clinical Policy: Enzalutamide (Xtandi)

Reference Number: HIM.PA.164
Effective Date: 03.01.22
Last Review Date: 02.22
Line of Business: HIM

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 (ADT) (*see Appendix D*);
   b. Metastatic CSPC;
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age ≥ 18 years;
4. For Xtandi request, medical justification supports inability to use generic enzalutamide, if available, (e.g., contraindications to excipients);
5. Prescribed concurrently with a gonadotropin-releasing hormone (GnRH) analog or member 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 or 1 tablet) per day;
   b. Dose does not exceed 160 mg (4 capsules or 2 tablets) 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 or 3 tablets) 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: 6 months

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): HIM.PA.154 for health insurance marketplace.

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. For Xtandi request, medical justification supports inability to use enzalutamide, if available, (e.g., contraindications to excipients);
4. 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 or 1 tablet) per day;
   b. New dose does not exceed 160 mg (4 capsules or 2 tablets) 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 or 3 tablets) 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: 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.
   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): HIM.PA.154 for health insurance marketplace.

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 – HIM.PA.154 for health insurance marketplace or evidence of coverage documents.

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

NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives
Not applicable

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, 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) agonist 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 (Eulexin®), nilutamide (Nilandron®), Xtandi® (enzalutamide), Erleada® (apalutamide)
    - LHRH antagonist: Firmagon® (degarelix), Orgovyx® (relugolix)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CRPC, metastatic CSPC	160 mg (two 80 mg tablets) 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
- Tablets: 40 mg, 80 mg

VII. References
1. Xtandi Prescribing Information. Northbrook, IL: Astellas Pharma US.; May 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/213674s002lbl.pdf. Accessed November 16, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at https://www.nccn.org/professionals/drug_compendium/content/. Accessed November 16, 2021.
3. National Comprehensive Cancer Network. Prostate Cancer Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed November 16, 2021.

4. Virgo KS, Basch E, Loblaw DA, et al. Second-Line Hormonal Therapy for Men with Chemotherapy-Naïve Castration-Resistant Prostate Cancer. American Society of Clinical Oncology (ASCO). Published online April 25, 2017, DOI: 10.1200/JCO.2017.72.8030. Available at: https://www.asco.org/practice-patients/guidelines/genitourinary-cancer#/25251. Accessed January 19, 2022.
5. Virgo KS, Rumble B, de Wit R, et al. Initial Management of Non-Castrate Advanced, Recurrent or Metastatic Prostate Cancer. American Society of Clinical Oncology (ASCO). Published ahead of print January 26, 2021, DOI: 10.1200/JCO.20.03256. Available at: https://www.asco.org/practice-patients/guidelines/genitourinary-cancer#/9521. Accessed January 19, 2022.
6. Basch E, Loblaw DA, Oliver TK, et al. Systemic Therapy in Men with Metastatic Castration-Resistant Prostate Cancer (CRPC). American Society of Clinical Oncology (ASCO). Published online before print September 8, 2014. Available at: https://www.asco.org/practice-patients/guidelines/genitourinary-cancer#/9496. Accessed January 19, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created per November SDC and prior clinical guidance (adapted from CP.PHAR.106).	11.30.21	02.22

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 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.

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