Clinical Policy: Enzalutamide (Xtandi)

Reference Number: PA.CP.PHAR.106
Effective Date: 01/18
Last Review Date: 04/19 Revision Log

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
It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Xtandi is **medically necessary** when one of 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 ≥ 18 years;
4. For non-metastatic disease, member will use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy;
5. 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: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies:
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: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

III. 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

Not applicable

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)

IV. 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

V. Product Availability

Capsule: 40 mg

VI. References

1. Xtandi Prescribing Information. Northbrook, IL: Astellas Pharma US.; July 2018. Available at: https://www.xtandi.com/. Accessed February 26, 2019.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. February 26, 2019.
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 February 26, 2019.
5. National Comprehensive Cancer Network. Prostate Cancer Version 01.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed February 26, 2019.

Reviews, Revisions, and Approvals	Date	Approval Date
Specialist requirement was added; off-label use in castration-naïve prostate cancer removed per NCCN guidelines; references reviewed and updated.	05.18	
2Q 2019 annual review: 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; added urologist prescriber option; references reviewed and updated.; references reviewed and updated.	04/19	