Clinical Policy Title:	enzalutamide
Policy Number:	RxA.318
Drug(s) Applied:	Xtandi®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of Business

Background

Enzalutamide (Xtandi®) is an androgen receptor inhibitor. It is indicated for the treatment of patients with castration-resistant prostate cancer (CRPC) and metastatic castration-sensitive prostate cancer(mCSPC).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
enzalutamide (Xtandi®)	CRPC	160 mg orally once daily	160 mg/day; 80 mg /day if taking with strong CYP2C8 inhibitor; 240 mg/day if taking a strong CYP3A4 inducer
	mCSPC	160 mg orally once daily	160 mg/day; 80 mg /day if taking with strong CYP2C8 inhibitor; 240 mg/day if taking a strong CYP3A4 inducer

Dosage Forms

- Capsule: 40 mg
- Tablet: 40 mg, 80 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Member has one of the following (a or b):
   a. Diagnosis of CRPC, as evidenced by disease progression despite bilateral orchiectomy or other androgen deprivation therapy (ADT) (*see Appendix D*);
   b. Diagnosis of metastatic CSPC;
2. Prescribed by or in consultation with an oncologist or urologist;

3. 18 years of age or older;
4. Member will use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy;
5. Dose does not exceed one of the following (a, b, or c):
   a. 80 mg per day (2 capsules per day) if prescribed concomitantly with a strong CYP2C8 inhibitor (e.g., gemfibrozil);
   b. 160 mg per day (4 capsules per day);
   c. 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);
   d. For any off-label dosing regimen, use 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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indications 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 one of the following (a, b, or c):
   a. 80 mg per day (2 capsules per day) if prescribed concomitantly with a strong CYP2C8 inhibitor (e.g., gemfibrozil);
   b. 160 mg per day (4 capsules per day);
   c. 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);
   d. For any off-label dosing regimen, use 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
Commercial: 6 months
Medicaid: 6 months

III. Appendices

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
mCSPC: Metastatic castration-sensitive prostate cancer

APPENDIX B: Therapeutic Alternatives

- Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):

- None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

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

References

1. Xtandi Prescribing Information. Northbrook, IL: Astellas Pharma US.; October 2020. Available at: https://www.xtandi.com/. Accessed April 15, 2021.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed April 15, 2021.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/ . Accessed April 15, 2021.
4. Enzalutamide. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org . Accessed April 15, 2021.
5. National Comprehensive Cancer Network. Prostate Cancer Version 02.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf . Accessed April 15, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established	01/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated. 2. Line of Business Policy Applies to was update to all lines of business. 3. Background was updated. 4. Dosing information updated to include metastatic castration-sensitive prostate cancer(mCSPC) dosing regimen. 5. Initial Approval criteria updated to include criteria for metastatic castration-sensitive prostate cancer(mCSPC). 6. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 7. Initial and continued approval duration for Medicaid was added; commercial approval duration was updated to 6	07/24/2020	09/14/2020

months. 8. APPENDIX A was updated to include metastatic castration-sensitive prostate cancer(mCSPC). 9. References were updated.		
Policy was reviewed: 1. Continued Therapy criteria II.A.1 was rephrased to " Member is currently receiving medication that has been authorized by RxAdvance..." 2. References were reviewed and revised. 3. Updated off-label dosing criteria under I.A.5 and II.A.3	04/15/2021	06/10/2021