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5.21.021

Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	October 4, 2012
Subject:	Xtandi	**Page:**	1 of 6

Last Review Date: December 13, 2024

Xtandi

Description

Xtandi (enzalutamide)

Background
Xtandi (enzalutamide) is an androgen receptor inhibitor used for the treatment of prostate cancer. Xtandi inhibits androgen binding to androgen receptors; and consequently, inhibits nuclear translocation of androgen receptors and their interaction with DNA. Xtandi decreases proliferation and induces cell death of prostate cancer cells (1).

Regulatory Status
FDA-approved indications: Xtandi is an androgen receptor inhibitor indicated for the treatment of patients with: (1)

- castration-resistant prostate cancer (CRPC).
- metastatic castration-sensitive prostate cancer (mCSPC).
- non-metastatic castration-sensitive prostate cancer (nmCSPC) with biochemical recurrence at high risk for metastasis (high-risk BCR).

Xtandi label includes warnings for seizures, posterior reversible encephalopathy syndrome (PRES), hypersensitivity, ischemic heart disease, falls and fractures, and embryo-fetal toxicity (1).

Discontinue Xtandi in patients who develop PRES or a seizure during treatment. Monitor patients for signs and symptoms of ischemic heart disease. Discontinue Xtandi for Grade 3-4 ischemic heart disease events. Evaluate patients for fracture and fall risk. Monitor and manage patients at risk for fractures and consider use of bone-targeted agents (1).

Xtandi can cause fetal harm and loss of pregnancy. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Xtandi and for 3 months after the last dose of Xtandi. Xtandi should not be handled by females who are or may become pregnant (1).

The safety and effectiveness of Xtandi in pediatric and female patients have not been established (1).

Related policies
Erleada, Nilandron, Nubeqa, Orgovyx, Yonsa, Zytiga

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Xtandi may be considered **medically necessary** if the conditions indicated below are met.

Xtandi may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Gender Male

Diagnoses

Patient must have **ONE** of the following:

1. Castration-resistant prostate cancer (CRPC)
    a. Patient is receiving gonadotropin-releasing hormone (GnRH) analog **OR** patient has had a bilateral orchiectomy
2. Metastatic castration-sensitive prostate cancer (mCSPC)
    a. Patient is receiving gonadotropin-releasing hormone (GnRH) analog **OR** patient has had a bilateral orchiectomy
3. Non-metastatic castration-sensitive prostate cancer (nmCSPC)
    a. Biochemical recurrence at high risk for metastasis (high-risk BCR)

AND ALL of the following for **ALL** indications:

1. **NO** dual therapy with another androgen receptor inhibitor (see Appendix 1)
2. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Xtandi and for 3 months after the last dose

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Strength	Quantity
40 mg	160 mg per day
80 mg	

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Xtandi (enzalutamide) is indicated for the treatment of patients with castration-resistant prostate cancer, metastatic castration-sensitive prostate cancer, and non-metastatic castration-sensitive prostate cancer with high-risk BCR. Xtandi label includes warnings for seizures, posterior reversible encephalopathy syndrome (PRES), hypersensitivity, ischemic heart disease, falls and fractures, and embryo-fetal toxicity. The safety and effectiveness of Xtandi in pediatric and female patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Xtandi while maintaining optimal therapeutic outcomes.

References

1. Xtandi [package insert]. Northbrook, IL: Astellas Pharma US; November 2023.
2. NCCN Drugs & Biologics Compendium® Enzalutamide 2024. National Comprehensive Cancer Network, Inc. Accessed on October 3, 2024.

Policy History

Date	Action/Reason
October 2012	New addition to PA
December 2012	Removal of prior docetaxel use requirement (based on expert opinion). Annual editorial review and update
March 2014	Annual review
March 2015	Annual editorial review and reference update
June 2016	Annual editorial review and reference update Policy number change from 5.04.21 to 5.21.21
March 2017	Annual editorial review and reference update Addition of no dual therapy with another androgen receptor inhibitor
June 2018	Annual editorial review and reference update
August 2018	Removal of metastatic prostate cancer requirement, addition of requirement of patient is receiving GnRH analog or patient has had bilateral orchiectomy, if patient or their partner are of child bearing age, the patient has been instructed to practice effective contraception during therapy and for 3 months after stopping therapy
September 2018	Annual editorial review
June 2019	Annual review
December 2019	Annual review
January 2020	Addition of the diagnosis metastatic castration-sensitive prostate cancer (mCSPC) to criteria
March 2020	Annual review
September 2020	Annual review. Revised quantity limits to include Xtandi tablets
March 2021	Annual editorial review and reference update
June 2021	Annual editorial review and reference update
December 2022	Annual review and reference update. Changed policy number to 5.21.021
December 2023	Annual review and reference update
January 2024	Per PI update, added indication of non-metastatic castration-sensitive prostate cancer with high-risk BCR. Also changed quantity limit to 160 mg per day and revised contraception wording for consistency

March 2024	Annual review and reference update
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.

Appendix 1 - List of Androgen Receptor Inhibitors

Generic Name	Brand Name
abiraterone	Yonsa
abiraterone	Zytiga
abiraterone/niraparib	Akeega
apalutamide	Erleada
darolutamide	Nubeqa
enzalutamide	Xtandi
nilutamide	Nilandron