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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Antineoplastic Agents	**Original Policy Date:**	October 4, 2012
Subject:	Xtandi	**Page:**	1 of 5

Last Review Date: March 12, 2021

Xtandi

Description

Xtandi (enzalutamide)

Background
Xtandi (enzalutamide) is indicated for men with castration-resistant prostate cancer (CRPC, prostate cancer that is resistant to medical or surgical treatments that lower testosterone) and metastatic castration-sensitive prostate cancer (mCSPC). Prostate cancer is an androgen-dependent disease. Xtandi targets multiple steps in the androgen receptor-signaling pathway, the major driver of prostate cancer growth. It works by competitively inhibiting androgen binding to androgen receptors and inhibits androgen receptor nuclear translocation and interaction with DNA (1).

Regulatory Status
FDA-approved indication: Xtandi is an androgen receptor inhibitor indicated for the treatment of patients with castration-resistant prostate cancer and metastatic castration-sensitive prostate cancer (mCSPC) (1).

Xtandi can cause fetal harm and potential loss of pregnancy. Advise males 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).

Seizure, ischemic heart disease, and falls and fractures may occur in patients receiving Xtandi. Advise patients of the risk of developing a seizure while receiving Xtandi. Permanently discontinue Xtandi in patients who develop a seizure during treatment. Monitor patients for signs

and symptoms of ischemic heart disease. Discontinue Xtandi for Grade 3-4 ischemic heart disease. Evaluate patients for fracture and fall risk. Monitor and manage patients at risk for fractures and consider use of bone-targeted agents (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** for male patients who are 18 years of age or older with a confirmed diagnosis of castration-resistant prostate cancer or metastatic castration-sensitive prostate cancer (mCSPC) and if the conditions indicated below are met.

Xtandi may be considered **investigational** in patients who are female, in patients less than 18 years of age, and 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)
2. Metastatic Castration-Sensitive Prostate Cancer (mCSPC)

AND ONE of the following for both indications:

1. Patient is receiving gonadotropin-releasing hormone (GnRH) analog
2. Patient has had a bilateral orchiectomy

AND ALL of the following:

1. **NO** dual therapy with another androgen receptor inhibitor (see Appendix 1)
2. Prescriber agrees to advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of Xtandi

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Strength	Quantity
40 mg	360 units per 90 days **OR**
80 mg	180 units per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Xtandi (enzalutamide) is FDA-approved for treatment of patients with castration-resistant prostate cancer (CRPC) or metastatic castration-sensitive prostate cancer (mCSPC). 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; October 2020.

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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.

Appendix 1 - List of Androgen Receptor Inhibitors

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