HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use XTANDI safely and effectively. See full prescribing information for XTANDI.

XTANDI® (enzalutamide) capsules, for oral use
XTANDI® (enzalutamide) tablets, for oral use
Initial U.S. Approval: 2012

RECENT MAJOR CHANGES

Dosage and Administration (2.1)	1/2025
Warnings and Precautions (5.7)	1/2025

INDICATIONS AND USAGE

XTANDI is an androgen receptor inhibitor indicated for the treatment of patients with:

- castration-resistant prostate cancer. (1)
- metastatic castration-sensitive prostate cancer. (1)
- non-metastatic castration-sensitive prostate cancer with biochemical recurrence at high risk for metastasis. (1)

DOSAGE AND ADMINISTRATION

- Take XTANDI 160 mg administered orally once daily with or without food. (2.1)
- Advise patients to take each capsule or tablet whole with a sufficient amount of water to ensure that all medication is successfully swallowed. (2.1, 5.7)
- Patients receiving XTANDI for castration-resistant prostate cancer, or metastatic castration sensitive prostate cancer should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy. (2.1)
- Patients with non-metastatic castration-sensitive prostate cancer with biochemical recurrence at high risk for metastasis may be treated with or without a GnRH analog. (2.1)

DOSAGE FORMS AND STRENGTHS

- Capsules: 40 mg (3)
- Tablets: 40 mg, 80 mg (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Seizure occurred in 0.6% of patients receiving XTANDI. In patients with predisposing factors, seizures were reported in 2.2% of patients. Permanently discontinue XTANDI in patients who develop a seizure during treatment. (5.1)
- Posterior reversible encephalopathy syndrome (PRES): Discontinue XTANDI. (5.2)
- Hypersensitivity: Discontinue XTANDI. (5.3)
- Ischemic Heart Disease: Optimize management of cardiovascular risk factors. Discontinue XTANDI for Grade 3-4 adverse reactions (5.4)
- Falls and Fractures: Evaluate patients for fracture and fall risk, and treat patients with bone-targeted agents according to established guidelines. (5.5)
- Embryo-Fetal Toxicity: XTANDI can cause fetal harm and loss of pregnancy. Advise males with female partners of reproductive potential to use effective contraception. (5.6, 8.1, 8.3)
- Severe Dysphagia or Choking Related to Product Size: Consider using smaller XTANDI tablet(s) in patients who have difficulty swallowing. Discontinue XTANDI for patients who cannot swallow capsules or tablets. (2.1, 5.7)

ADVERSE REACTIONS

The most common adverse reactions (≥ 10%) that occurred more frequently (≥ 2% over placebo) in the XTANDI-treated patients are musculoskeletal pain, fatigue, hot flush, constipation, decreased appetite, diarrhea, hypertension, hemorrhage, fall, fracture, and headache. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Astellas Pharma US, Inc. at 1-800-727-7003 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Strong CYP2C8 Inhibitors: Avoid strong CYP2C8 inhibitors. If coadministration cannot be avoided, reduce the dosage of XTANDI. (2.3, 7.1)
- Strong CYP3A4 Inducers: Avoid strong CYP3A4 inducers. If coadministration cannot be avoided, increase the dosage of XTANDI. (2.3, 7.1)
- Avoid coadministration with certain CYP3A4, CYP2C9, or CYP2C19 substrates for which a minimal decrease in concentration may lead to therapeutic failure of the substrate. In cases where active metabolites are formed, there may be increased exposure to the active metabolites. (7.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 3/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Recommended Dosage
2.2 Dosage Modifications for Adverse Reactions
2.3 Dosage Modifications for Drug Interactions
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Seizure
5.2 Posterior Reversible Encephalopathy Syndrome (PRES)
5.3 Hypersensitivity
5.4 Ischemic Heart Disease
5.5 Falls and Fractures
5.6 Embryo-Fetal Toxicity
5.7 Dysphagia or Choking
6 ADVERSE REACTIONS
6.1 Clinical Trial Experience
6.2 Post-Marketing Experience
7 DRUG INTERACTIONS
7.1 Effect of Other Drugs on XTANDI
7.2 Effect of XTANDI on Other Drugs
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.3 Females and Males of Reproductive Potential
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Renal Impairment
8.7 Hepatic Impairment
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

XTANDI® is indicated for the treatment of patients with:

- 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)

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage of XTANDI is 160 mg administered orally once daily with or without food *[see Clinical Pharmacology (12.3)]* until disease progression or unacceptable toxicity.

Advise patients to take each capsule or tablet whole with a sufficient amount of water to ensure that all medication is successfully swallowed. Do NOT chew, dissolve, or open the capsules. Do NOT cut, crush, or chew the tablets.

Patients with CRPC or mCSPC receiving XTANDI should also receive a gonadotropic-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

Patients with nmCSPC with high-risk BCR may be treated with XTANDI with or without a GnRH analog. For patients who receive XTANDI with or without a GnRH analog, treatment can be suspended if PSA is undetectable (< 0.2 ng/mL) after 36 weeks of therapy. Reinitiate treatment when PSA has increased to ≥ 2.0 ng/mL for patients who had prior radical prostatectomy or ≥ 5.0 ng/mL for patients who had prior primary radiation therapy *[see Clinical Studies (14)]*.

2.2 Dosage Modifications for Adverse Reactions

If a patient experiences a ≥ Grade 3 or an intolerable adverse reaction, withhold XTANDI for one week or until symptoms improve to ≤ Grade 2, then resume at the same or a reduced dose (120 mg or 80 mg) if warranted *[see Warnings and Precautions (5.1, 5.2)]*.

2.3 Dosage Modifications for Drug Interactions

Strong CYP2C8 Inhibitors

Avoid the coadministration of strong CYP2C8 inhibitors. If the coadministration of a strong CYP2C8 inhibitor cannot be avoided, reduce the XTANDI dosage to 80 mg once daily. If the coadministration of the strong inhibitor is discontinued, increase the XTANDI dosage to the dosage used prior to initiation of the strong CYP2C8 inhibitor *[see Clinical Pharmacology (12.3)]*.

Strong CYP3A4 Inducers

Avoid the coadministration of strong CYP3A4 inducers. If the coadministration of a strong CYP3A4 inducer cannot be avoided, increase the XTANDI dosage from 160 mg to 240 mg orally once daily. If the coadministration of the strong CYP3A4 inducer is discontinued, decrease the XTANDI dosage to the dosage used prior to initiation of the strong CYP3A4 inducer *[see Clinical Pharmacology (12.3)]*.