Xtandi® (enzalutamide)

40 mg tablets | 80 mg tablets

XTANDI is indicated for the treatment of patients with castration-resistant prostate cancer (CRPC) or metastatic castration-sensitive prostate cancer (mCSPC).[1]

XTANDI is the first and only novel hormone therapy approved by the FDA in 3 advanced prostate cancer disease states—**mCSPC**, **nmCRPC**, and **mCRPC**[1]

	mCSPC	nmCRPC	mCRPC		
	2019 New indication[2]	2018 New indication[3]	2012 Initial approval[5]	2014 New indication[7]	2016 Label update[8]
	ARCHES TRIAL[1]	PROSPER TRIAL[1,4]	AFFIRM TRIAL[1,6]	PREVAIL TRIAL[1]	TERRAIN TRIAL[1,4]
Patient Enrollment	1150	1401	1199	1717	375
Treatment	XTANDI + LHRH therapy*	XTANDI + LHRH therapy*	XTANDI + LHRH therapy*	XTANDI + LHRH therapy*	XTANDI + LHRH therapy*
Comparator	Placebo + LHRH therapy*	Placebo + LHRH therapy*	Placebo + LHRH therapy*	Placebo + LHRH therapy*	Bicalutamide + LHRH therapy*
Chemotherapy	• Prior docetaxel use allowed • Docetaxel-naive allowed	Chemotherapy-naive	Prior docetaxel-based therapy use required	Chemotherapy-naive	Chemotherapy-naive
ECOG Status	0-1	0-1	0-2	0-1	0-1

To learn more, please visit **XtandiHCP.com**

XTANDI has a long history of clinical data and a decade of prescribed use[1]

#1 PRESCRIBED BRANDED NOVEL HORMONE THERAPY IN mCSPC AND CRPC†[4]

†Based on IQVIA Global Syndicated Prostate Cancer Tracker, patient share captured among oncologists' and urologists' mCSPC patients, August 2022.[4]
THIS INFORMATION DOES NOT IMPLY SAFETY OR EFFICACY OF ANY PRODUCT; NO COMPARISONS SHOULD BE MADE.

More than 254,000 patients prescribed

XTANDI since FDA approval—and counting‡[1,4]

‡Estimate based on U.S. sales and use data from September 2012 to July 2022.[4,5]

5 clinical trials[1]

5842 patients enrolled across all 5 trials[1]

10 years in the market[5]

Select Safety Information

Seizure occurred in 0.5% of patients receiving XTANDI in seven randomized clinical trials. In a study of patients with predisposing factors for seizure, 2.2% of XTANDI-treated patients experienced a seizure. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Patients in the study had one or more of the following predisposing factors: use of medications that may lower the seizure threshold, history of traumatic brain or head injury, history of cerebrovascular accident or transient ischemic attack, and Alzheimer's disease, meningioma, or leptomeningeal disease from prostate cancer, unexplained loss of consciousness within the last 12 months, history of seizure, presence of a space occupying lesion of the brain, history of arteriovenous malformation, or history of brain infection. Advise patients of the risk of developing a seizure while taking XTANDI and of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

Please click here for Important Safety Information on page 2 and accompanying Full Prescribing Information.

Metastatic castration-sensitive prostate cancer is defined as metastatic disease in patients who have not yet received, or who have received and can still respond to, androgen deprivation therapy (LHRH therapy or prior bilateral orchiectomy).[9]
Castration-resistant prostate cancer is defined as disease progression on androgen deprivation therapy (LHRH therapy or prior bilateral orchiectomy) despite castrate levels of testosterone.[10]

ECOG, Eastern Cooperative Oncology Group; **LHRH**, luteinizing hormone-releasing hormone; **mCRPC**, metastatic castration-resistant prostate cancer; **NBRx**, new-to-brand; **nmCRPC**, nonmetastatic castration-resistant prostate cancer; **PSA**, prostate-specific antigen.

***Or after bilateral orchiectomy.[1]**

Indications

XTANDI (enzalutamide) is indicated for the treatment of patients with:

- castration-resistant prostate cancer (CRPC)
- metastatic castration-sensitive prostate cancer (mCSPC)

Important Safety Information

Warnings and Precautions

Seizure occurred in 0.5% of patients receiving XTANDI in seven randomized clinical trials. In a study of patients with predisposing factors for seizure, 2.2% of XTANDI-treated patients experienced a seizure. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Patients in the study had one or more of the following predisposing factors: use of medications that may lower the seizure threshold, history of traumatic brain or head injury, history of cerebrovascular accident or transient ischemic attack, and Alzheimer's disease, meningioma, or leptomeningeal disease from prostate cancer, unexplained loss of consciousness within the last 12 months, history of seizure, presence of a space occupying lesion of the brain, history of arteriovenous malformation, or history of brain infection. Advise patients of the risk of developing a seizure while taking XTANDI and of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

Posterior Reversible Encephalopathy Syndrome (PRES)
There have been reports of PRES in patients receiving XTANDI. PRES is a neurological disorder that can present with rapidly evolving symptoms including seizure, headache, lethargy, confusion, blindness, and other visual and neurological disturbances, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably MRI. Discontinue XTANDI in patients who develop PRES.

Hypersensitivity reactions, including edema of the face (0.5%), tongue (0.1%), or lip (0.1%) have been observed with XTANDI in seven randomized clinical trials. Pharyngeal edema has been reported in post-marketing cases. Advise patients who experience any symptoms of hypersensitivity to temporarily discontinue XTANDI and promptly seek medical care. Permanently discontinue XTANDI for serious hypersensitivity reactions.

Ischemic Heart Disease In the combined data of four randomized, placebo-controlled clinical studies, ischemic heart disease occurred more commonly in patients on the XTANDI arm compared to patients on the placebo arm (2.9% vs 1.3%). Grade 3-4 ischemic events occurred in 1.4% of patients on XTANDI versus 0.7% on placebo. Ischemic events led to death in 0.4% of patients on XTANDI compared to 0.1% on placebo. Monitor for signs and symptoms of ischemic heart disease. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Discontinue XTANDI for Grade 3-4 ischemic heart disease.

Falls and Fractures occurred in patients receiving XTANDI. Evaluate patients for fracture and fall risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents. In the combined data of four randomized, placebo-controlled clinical studies, falls occurred in 11% of patients treated with XTANDI compared to 4% of patients treated with placebo. Fractures occurred in 10% of patients treated with XTANDI and in 4% of patients treated with placebo.

Embryo-Fetal Toxicity The safety and efficacy of XTANDI have not been established in females. XTANDI can cause fetal harm and loss of pregnancy when administered to a pregnant female. 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.

Adverse Reactions (ARs)

In the data from the four randomized placebo-controlled trials, the most common ARs (≥ 10%) that occurred more frequently (≥ 2% over placebo) in XTANDI-treated patients were asthenia/fatigue, back pain, hot flush, constipation, arthralgia, decreased appetite, diarrhea, and hypertension. In the bicalutamide-controlled study, the most common ARs (≥ 10%) reported in XTANDI-treated patients were asthenia/fatigue, back pain, musculoskeletal pain, hot flush, hypertension, nausea, constipation, diarrhea, upper respiratory tract infection, and weight loss.

In AFFIRM, the placebo-controlled study of metastatic CRPC (mCRPC) patients who previously received docetaxel, Grade 3 and higher ARs were reported among 47% of XTANDI-treated patients. Discontinuations due to adverse events (AEs) were reported for 16% of XTANDI-treated patients. In PREVAIL, the placebo-controlled study of chemotherapy-naive mCRPC patients, Grade 3-4 ARs were reported in 44% of XTANDI patients and 37% of placebo patients. Discontinuations due to AEs were reported for 6% of XTANDI-treated patients. In TERRAIN, the bicalutamide-controlled study of chemotherapy-naive mCRPC patients, Grade 3-4 ARs were reported in 39% of XTANDI patients and 38% of bicalutamide patients. Discontinuations with an AE as the primary reason were reported for 8% of XTANDI patients and 6% of bicalutamide patients.

In PROSPER, the placebo-controlled study of non-metastatic CRPC (nmCRPC) patients, Grade 3 or higher ARs were reported in 31% of XTANDI patients and 23% of placebo patients. Discontinuations with an AE as the primary reason were reported for 9% of XTANDI patients and 6% of placebo patients.

In ARCHES, the placebo-controlled study of metastatic CSPC (mCSPC) patients, Grade 3 or higher AEs were reported in 24% of XTANDI-treated patients. Permanent discontinuation due to AEs as the primary reason was reported in 5% of XTANDI patients and 4% of placebo patients.

Lab Abnormalities: Lab abnormalities that occurred in ≥ 5% of patients, and more frequently (> 2%) in the XTANDI arm compared to placebo in the pooled, randomized, placebo-controlled studies are neutrophil count decreased, white blood cell decreased, hyperglycemia, hypermagnesemia, hyponatremia, and hypercalcemia.

Hypertension: In the combined data from four randomized placebo-controlled clinical trials, hypertension was reported in 12% of XTANDI patients and 5% of placebo patients. Hypertension led to study discontinuation in < 1% of patients in each arm.

Drug Interactions

Effect of Other Drugs on XTANDI Avoid coadministration with strong CYP2C8 inhibitors. If coadministration cannot be avoided, reduce the dosage of XTANDI.

Avoid coadministration with strong CYP3A4 inducers. If coadministration cannot be avoided, increase the dosage of XTANDI.

Effect of XTANDI on Other Drugs Avoid coadministration with certain CYP3A4, CYP2C9, and CYP2C19 substrates for which minimal decrease in concentration may lead to therapeutic failure of the substrate. If coadministration cannot be avoided, increase the dosage of these substrates in accordance with their Prescribing Information. In cases where active metabolites are formed, there may be increased exposure to the active metabolites.

Please click here for accompanying Full Prescribing Information.

References: 1. XTANDI [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** U.S. Food and Drug Administration. Xtandi sNDA 203415/S-015 (ARCHES) approval letter (12-16-2019). https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2019/203415Orig1s015ltr.pdf. Accessed 09-07-2022. **3.** U.S. Food and Drug Administration. Xtandi sNDA 203415/S-014 (PROSPER) approval letter (07-13-2018). https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/203415Orig1s014ltr.pdf. Accessed 01-18-2022. **4.** Astellas and Pfizer. XTANDI. Data on File. **5.** U.S. Food and Drug Administration. Xtandi NDA 203415 approval letter (08-31-2012). https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2012/203415Orig1s000ltr.pdf. Accessed 06-16-2022. **6.** Scher HI, Fizazi K, Saad F, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. N Engl J Med 2012;367(13):1187-97. **7.** U.S. Food and Drug Administration. Xtandi sNDA 203415/S-003 (PREVAIL) approval letter (09-10-2014). https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2014/203415Orig1s003ltr.pdf. Accessed 12-05-2022. **8.** U.S. Food and Drug Administration. Xtandi sNDA 203415/S-009 (TERRAIN) approval letter (10-20-2016). https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2016/203415Orig1s009ltr.pdf. Accessed 12-05-2022. **9.** Armstrong AJ, Szmulewitz RZ, Petrylak DP, et al. ARCHES: a randomized, phase III study of androgen deprivation therapy with enzalutamide or placebo in men with metastatic hormone-sensitive prostate cancer. J Clin Oncol 2019;37(32):2974-86. **10.** Eisenberger MA, Saad F. Introduction-castration resistant prostate cancer: a rapidly expanding clinical state and a model for new therapeutic opportunities. In: Saad F, Eisenberger MA, eds. Management of Castration Resistant Prostate Cancer. 1st ed. New York, NY: Springer, 2014:3-8.

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Pfizer Oncology

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