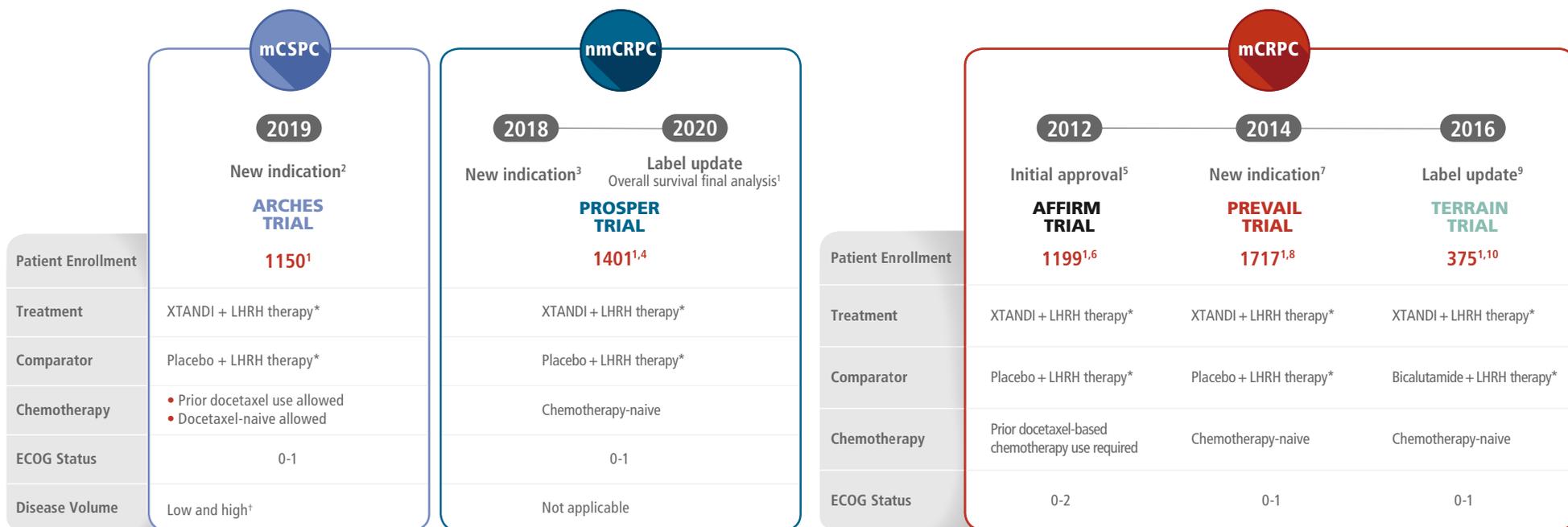


XTANDI is the first and only novel hormone therapy approved by the FDA in 3 patient types in advanced prostate cancer—**metastatic castration-sensitive prostate cancer (mCSPC), nonmetastatic castration-resistant prostate cancer (nmCRPC), and metastatic castration-resistant prostate cancer (mCRPC)**¹



5842
enrolled across
all 5 trials¹



8
years in
the market⁵



5
clinical
trials¹

Since FDA approval in 2012, XTANDI has been prescribed to **180,000 patients—and counting**⁴

Visit XtandiHCP.com to learn more

Indications

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

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

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.

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).¹¹

Castration-resistant prostate cancer is defined as disease progression on androgen deprivation therapy (LHRH therapy or prior bilateral orchiectomy).¹²

ECOG, Eastern Cooperative Oncology Group; LHRH, luteinizing hormone-releasing hormone.

*Or after bilateral orchiectomy.¹

†Defined as metastases involving the viscera or, in the absence of visceral lesions, ≥ 4 bone lesions, ≥ 1 of which must be in a bony structure beyond the vertebral column and pelvic bone.¹

‡Estimate based on US sales and use data from September 2012 to July 2020.⁴

Please see [Important Safety Information](#) and [Full Prescribing Information](#).

Indications

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Important Safety Information

Warnings and Precautions

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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 ($\geq 10\%$) that occurred more frequently ($\geq 2\%$ 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 ($\geq 10\%$) 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 $\geq 5\%$ 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 strong CYP2C8 inhibitors, as they can increase the plasma exposure to XTANDI. If co-administration is necessary, reduce the dose of XTANDI.

Avoid strong CYP3A4 inducers as they can decrease the plasma exposure to XTANDI. If co-administration is necessary, increase the dose of XTANDI.

Effect of XTANDI on Other Drugs Avoid CYP3A4, CYP2C9, and CYP2C19 substrates with a narrow therapeutic index, as XTANDI may decrease the plasma exposures of these drugs. If XTANDI is co-administered with warfarin (CYP2C9 substrate), conduct additional INR monitoring.

Please see [Full Prescribing Information](#).

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 **Xtandi**[®]
(enzalutamide)
40 mg tablets | 80 mg tablets

