XTANDI® (enzalutamide) was approved by the Food and Drug Administration (FDA) for the treatment of a type of prostate cancer that: no longer responds to a medical or surgical treatment that lowers testosterone, and has spread, or metastasized, beyond the prostate to other parts of the body.¹

**HELPFUL INFORMATION ABOUT XTANDI DOSING**

- The recommended dose of XTANDI is four 40 mg capsules (160 mg) taken once a day, at the same time each day¹
- XTANDI can be taken with or without food¹
- Steroids, for example oral prednisone, can be taken but are not required with XTANDI*²
- XTANDI is taken with hormone therapy injections***

**HOW XTANDI WORKS**

Metastatic CRPC refers to when the cancer spreads outside the prostate and progresses despite treatment.⁴ That’s why a doctor may recommend an additional medication like XTANDI to help treat metastatic CRPC.

In prostate cancer, the androgen receptor (AR) is a key driver of progression.⁵ XTANDI is an AR-binding inhibitor, which works by preventing testosterone from binding to prostate cancer cells.² XTANDI is thought to act on multiple steps of the AR-signaling pathway within the tumor cells in vitro.¹

**SELECT SAFETY INFORMATION**

Contraindications: XTANDI is not indicated for use in women. XTANDI can cause fetal harm and potential loss of pregnancy.

Effect of XTANDI on Other Drugs: XTANDI is a strong CYP3A4 inducer and a moderate CYP2C9 and CYP2C19 inducer in humans. 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.

*In the PREVAIL trial, 27% of patients in the XTANDI arm and 30% of patients in the placebo arm received glucocorticoids for varying reasons. In the AFFIRM trial, 48% of patients in the XTANDI arm and 46% of patients in the placebo arm received glucocorticoids.

**Or after surgical castration.
SELECT SAFETY INFORMATION

Seizure occurred in 0.5% of patients receiving XTANDI in clinical studies. In a study of patients with predisposing factors, seizures were reported in 2.2% of patients. See section 5.1 of the Prescribing Information for the list of predisposing factors. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

There have been post approval reports of posterior reversible encephalopathy syndrome (PRES), a neurological disorder that can present with rapidly evolving symptoms and requires confirmation by brain imaging. Discontinue XTANDI in patients who develop PRES.

*Hazard ratio (HR) indicates the relative risk of a complication based on comparison of event rates between treatment and control.
**Contraindications** XTANDI is not indicated for women. XTANDI can cause fetal harm and potential loss of pregnancy.

**Warnings and Precautions** Seizure occurred in 0.5% of patients receiving XTANDI in clinical studies. In a study of patients with predisposing factors, seizures were reported in 2.2% of patients. See section 5.1 of the Prescribing Information for the list of predisposing factors. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

**Posterior Reversible Encephalopathy Syndrome (PRES)** In post approval use, there have been reports of PRES in patients receiving XTANDI. PRES is a neurological disorder which 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.

**Adverse Reactions** The most common adverse reactions (≥ 10%) that occurred more commonly (≥ 2% over placebo) in the XTANDI patients from the two placebo-controlled clinical trials were asthenia/fatigue, back pain, decreased appetite, constipation, arthralgia, diarrhea, hot flush, upper respiratory tract infection, peripheral edema, dyspnea, musculoskeletal pain, weight decreased, headache, hypertension, and dizziness/vertigo. In the bicalutamide-controlled study of chemotherapy-naïve patients, the most common adverse reactions (≥ 10%) reported in XTANDI patients were asthenia/fatigue, back pain, musculoskeletal pain, hot flush, hypertension, nausea, constipation, upper respiratory tract infection, diarrhea, and weight loss.

In the placebo-controlled study of patients taking XTANDI who previously received docetaxel, Grade 3 and higher adverse reactions were reported among 47% of XTANDI patients and 53% of placebo patients. Discontinuations due to adverse events were reported for 16% of XTANDI patients and 18% of placebo patients. In the placebo-controlled study of chemotherapy-naïve patients, Grade 3-4 adverse reactions were reported in 44% of XTANDI patients and 37% of placebo patients. Discontinuations due to adverse events were reported for 6% of both study groups. In the bicalutamide-controlled study of chemotherapy-naïve patients, Grade 3-4 adverse reactions were reported in 38.8% of XTANDI patients and 37.6% of bicalutamide patients. Discontinuations due to adverse events were reported for 7.6% of XTANDI patients and 6.3% of bicalutamide patients.

**Lab Abnormalities** In the two placebo-controlled trials, Grade 1-4 neutropenia occurred in 15% of XTANDI patients (1% Grade 3-4) and 6% of placebo patients (0.5% Grade 3-4). Grade 1-4 thrombocytopenia occurred in 6% of XTANDI patients (0.3% Grade 3-4) and 5% of placebo patients (0.5% Grade 3-4). Grade 1-4 elevations in ALT occurred in 10% of XTANDI patients (0.2% Grade 3-4) and 16% of placebo patients (0.2% Grade 3-4). Grade 1-4 elevations in bilirubin occurred in 3% of XTANDI patients (0.1% Grade 3-4) and 2% of placebo patients (no Grade 3-4).

**Infections** In the study of patients taking XTANDI who previously received docetaxel, 1% of XTANDI patients compared to 0.3% of placebo patients died from infections or sepsis. In the study of chemotherapy-naïve patients, 1 patient in each treatment group (0.1%) had an infection resulting in death.

**Falls** (including fall-related injuries) occurred in 9% of XTANDI patients and 4% of placebo patients in the two placebo-controlled trials. Falls were not associated with loss of consciousness or seizure. Fall-related injuries were more severe in XTANDI patients, and included non-pathologic fractures, joint injuries, and hematomas.

**Hypertension** occurred in 11% of XTANDI patients and 4% of placebo patients in the two placebo-controlled trials. No patients experienced hypertensive crisis. Medical history of hypertension was balanced between arms. 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 for additional safety information.
XTANDI® (enazalutamide) Capsules: A Treatment Option for Metastatic Castration-Resistant Prostate Cancer (CRPC)

References