Xtandi® (enzalutamide) capsules

DOSING INFORMATION

XTANDI (enzalutamide) capsules is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) who have previously received docetaxel.[1]

Capsules shown actual size.

- **Oral, once-daily XTANDI is administered as 160 mg, in four 40 mg capsules**[1]
  - Each capsule should be swallowed whole. Patients should not chew, dissolve, or open the capsules
- **XTANDI can be taken with or without food**[1]
- **Patients were allowed, but not required, to take glucocorticoids**[1]
  - In the clinical trial, 48% of patients in the XTANDI arm and 46% of patients in the placebo arm received glucocorticoids[1]

Use in specific populations	No dose adjustment of XTANDI is necessary for • Patients with mild to moderate hepatic impairment[1] • Patients with mild to moderate renal impairment[1] XTANDI has not been evaluated in • Patients with baseline severe hepatic impairment (Child-Pugh C)[1] • Patients with severe renal impairment, or end-stage renal disease[1]
Dose modifications	If a patient experiences a ≥ grade 3 toxicity or an intolerable side effect, withhold dosing for 1 week or until symptoms improve to ≤ grade 2, then resume at the same or a reduced dose (120 mg or 80 mg), if warranted.[1] The concomitant use of strong CYP2C8 inhibitors should be avoided if possible. If patients must be coadministered a strong CYP2C8 inhibitor, reduce the XTANDI dose to 80 mg once daily. If coadministration of the strong inhibitor is discontinued, the XTANDI dose should be returned to the dose used prior to initiation of the strong CYP2C8 inhibitor.[1]
What to do if a dose of XTANDI is missed	If a dose of XTANDI is missed, inform patients that they should take it as soon as they remember.[1] • If patients forget to take the dose for the whole day, they should take their normal dose the next day • Patients should not take more than their prescribed daily dose
Drug interactions with XTANDI	• Avoid strong CYP2C8 inhibitors, as they can increase the plasma exposure to XTANDI. If coadministration is necessary, reduce the dose of XTANDI to 80 mg once daily[1] • Avoid strong or moderate CYP3A4 or CYP2C8 inducers as they can alter the plasma exposure to XTANDI[1] • Avoid CYP3A4, CYP2C9, and CYP2C19 substrates with a narrow therapeutic index, as XTANDI may decrease the plasma exposures of these drugs. If XTANDI is coadministered with warfarin (CYP2C9 substrate), conduct additional INR monitoring[1]

Please see Important Safety Information on next page and Full Prescribing Information at XtandiHCP.com.

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Important Safety Information

Contraindications XTANDI can cause fetal harm when administered to a pregnant woman based on its mechanism of action. XTANDI is not indicated for use in women. XTANDI is contraindicated in women who are or may become pregnant.

Warnings and Precautions In the randomized clinical trial, seizure occurred in 0.9% of patients on XTANDI. No patients on the placebo arm experienced seizure. Patients experiencing a seizure were permanently discontinued from therapy. All seizures resolved. Patients with a history of seizure, taking medications known to decrease the seizure threshold, or with other risk factors for seizure were excluded from the clinical trial. Because of the risk of seizure associated with XTANDI use, patients should be advised of the risk of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others.

Adverse Reactions The most common adverse drug reactions (≥ 5%) reported in patients receiving XTANDI in the randomized clinical trial were asthenia/fatigue, back pain, diarrhea, arthralgia, hot flush, peripheral edema, musculoskeletal pain, headache, upper respiratory infection, muscular weakness, dizziness, insomnia, lower respiratory infection, spinal cord compression and cauda equina syndrome, hematuria, paresthesia, anxiety, and hypertension. Grade 1-4 neutropenia occurred in 15% of XTANDI patients (1% grade 3-4) and in 6% of patients on placebo (no grade 3-4). Grade 1-4 elevations in bilirubin occurred in 3% of XTANDI patients and 2% of patients on placebo. One percent of XTANDI patients compared to 0.3% of patients on placebo died from infections or sepsis. Falls or injuries related to falls occurred in 4.6% of XTANDI patients vs 1.3% of patients on placebo. 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. Grade 1 or 2 hallucinations occurred in 1.6% of XTANDI patients and 0.3% of patients on placebo, with the majority on opioid-containing medications at the time of the event.

Drug Interactions: Effect of Other Drugs on XTANDI Administration of strong CYP2C8 inhibitors can increase the plasma exposure to XTANDI. Coadministration of XTANDI with strong CYP2C8 inhibitors should be avoided if possible. If coadministration of XTANDI cannot be avoided, reduce the dose of XTANDI. Coadministration of XTANDI with strong or moderate CYP3A4 and CYP2C8 inducers can alter the plasma exposure of XTANDI and should be avoided if possible.
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 coadministered with warfarin (CYP2C9 substrate), conduct additional INR monitoring.

Please see Full Prescribing Information at XtandiHCP.com for complete safety information.

astellas
Leading Light for Life

MEDIVATION
Driven by science. Focused on life.

For more information about XTANDI, snap the QR code to visit XtandiHCP.com.

Reference: 1. XTANDI [prescribing information]. Northbrook, IL: Astellas Pharma US, Inc; 2012.