Xtandi®
(enzalutamide)
40 mg tablets | 80 mg tablets

Therapy Management Guide

Indications

XTANDI® is indicated for the treatment of patients with:

- nonmetastatic castration-sensitive prostate cancer (nmCSPC) with biochemical recurrence at high risk for metastasis (high-risk BCR)
- metastatic castration-sensitive prostate cancer (mCSPC)
- castration-resistant prostate cancer (CRPC)

The Warnings and Precautions for XTANDI include Seizure, Posterior Reversible Encephalopathy Syndrome (PRES), Hypersensitivity, Ischemic Heart Disease, Falls and Fractures, and Embryo-Fetal Toxicity.[1]

Please see Important Safety Information, including additional information about these Warnings and Precautions, throughout. Please see Full Prescribing Information in the pocket.
For more information, please visit xtandihcp.com.

Starting on XTANDI[1]

Indications

XTANDI is indicated for the treatment of patients with:

- nonmetastatic castration-sensitive prostate cancer (nmCSPC) with biochemical recurrence at high risk for metastasis (high-risk BCR)
- metastatic castration-sensitive prostate cancer (mCSPC)
- castration-resistant prostate cancer (CRPC)

XTANDI Dosage Forms and Strengths

40 mg tablets

80 mg tablets

40 mg capsules

Not actual size.

Recommended XTANDI Dosing

The recommended dosage of XTANDI is 160 mg administered orally once daily

Not actual size of tablets and penny.

	Recommended XTANDI Dosing		Administration Notes
For patients with nmCSPC with high-risk BCR	160 mg	by mouth once daily	Patients may be treated with XTANDI with or without a GnRH analog
For patients with mCSPC or CRPC who have undergone a bilateral orchiectomy	160 mg	by mouth once daily	
For patients with CRPC or mCSPC who have NOT undergone a bilateral orchiectomy	160 mg	by mouth once daily	Patients should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently

Important Safety Information
Warnings and Precautions

Seizure occurred in 0.6% of patients receiving XTANDI in eight 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.

Starting on XTANDI[1] (cont'd)

Dosage & Administration Patient Counseling	
Concomitant Treatments	• Discuss with patients with nmCSPC with high-risk BCR that they may be treated with or without GnRH therapy • Inform patients with CRPC or mCSPC, who have not undergone bilateral orchiectomy and are receiving GnRH therapy that they need to maintain this treatment during the course of treatment with XTANDI
Administration	• Instruct patients to take their dose at the same time each day (once daily) • XTANDI can be taken with or without food • Each capsule or tablet should be swallowed whole – Do not chew, dissolve, or open the capsules – Do not cut, crush, or chew the tablets
Treatment Suspension for Patients with nmCSPC with High-risk BCR	• For patients who receive XTANDI with or without a GnRH analog, treatment can be suspended if prostate-specific antigen (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
Dose Interruptions or Modifications	• Inform patients that they should not interrupt, modify the dose, or stop XTANDI without first consulting their healthcare provider
Missed Dose	• Inform patients that if they miss a dose, then they should take it as soon as they remember • If they forget to take the dose for the whole day, then they should take their normal dose the next day • They should not take more than their prescribed dose per day

Important Safety Information
Warnings and Precautions

Hypersensitivity reactions, including edema of the face (0.5%), tongue (0.1%), or lip (0.1%) have been observed with XTANDI in eight 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 five randomized, placebo-controlled clinical studies, ischemic heart disease occurred more commonly in patients on the XTANDI arm compared to patients on the placebo arm (3.5% vs 2%). Grade 3-4 ischemic events occurred in 1.8% of patients on XTANDI versus 1.1% 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.

Reference

1. XTANDI [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

Dosage Modifications[1]

XTANDI Dosage Modifications for Grade ≥ 3 or Intolerable Adverse Reactions

Withhold XTANDI

Withhold for 1 week **OR** Withhold until symptoms improve to ≤ Grade 2

Resume XTANDI

Resume at the **same dose** **OR** Resume at a **reduced dose if warranted (120 mg or 80 mg)**

XTANDI Dosage Modifications for Drug Interactions

XTANDI **&** a **Strong CYP2C8 Inhibitor** (e.g., gemfibrozil*)	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
XTANDI **&** a **Strong CYP3A4 Inducer** (e.g., rifampin*)	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

*Not an exhaustive list of strong inducers/inhibitors.

- **For patients with renal impairment:** No dosage modification is recommended for patients with mild to moderate renal impairment (creatinine clearance [CrCl] ≥ 30 mL/min). XTANDI has not been studied in patients with severe renal impairment (CrCl < 30 mL/min) or end-stage renal disease
- **For patients with hepatic impairment:** No dosage modification is recommended for patients with mild, moderate, or severe hepatic impairment

Important Safety Information
Warnings and Precautions

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 five randomized, placebo-controlled clinical studies, falls occurred in 12% of patients treated with XTANDI compared to 6% of patients treated with placebo. Fractures occurred in 13% of patients treated with XTANDI and in 6% of patients treated with placebo.

Dosage Modifications[1] (cont'd)

Effect of XTANDI on Other Drugs

XTANDI is a strong CYP3A4 inducer and a moderate CYP2C9 and CYP2C19 inducer

The coadministration of XTANDI decreases the concentrations of certain CYP3A4, CYP2C9, or CYP2C19 substrates, which may reduce the efficacy of these substrates (e.g., midazolam, S-warfarin, omeprazole*)	Avoid the coadministration of XTANDI with certain CYP3A4, CYP2C9, or CYP2C19 substrates for which a minimal decrease in concentration may lead to therapeutic failure of the substrate	If the 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

*Not an exhaustive list of substrates.

XTANDI Discontinuation Guidance[1]

Seizure

- 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

Posterior Reversible Encephalopathy Syndrome (PRES)

- Discontinue XTANDI in patients who develop PRES

Hypersensitivity

- 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

- Optimize management of cardiovascular risk factors
- Discontinue XTANDI for Grade 3-4 ischemic heart disease

See additional information about these Warnings and Precautions on the following pages

Important Safety Information
Warnings and Precautions

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.

Reference

1. XTANDI [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

Patient Counseling Information[1]*

The information contained in this brochure does not constitute medical advice and is not intended to replace a healthcare provider's independent medical judgment regarding treatment management of individual patients

*The data in WARNINGS and PRECAUTIONS reflect 8 randomized, controlled trials [AFFIRM, PREVAIL, TERRAIN, PROSPER, ARCHES, EMBARK, Asian PREVAIL (NCT02294461), and STRIVE (NCT01664923)] that were pooled to conduct safety analyses in patients with CRPC (N = 3651), mCSPC (N = 752), or nmCSPC with high-risk BCR (n = 707) treated with XTANDI. Patients received XTANDI 160 mg (N = 5110) or placebo orally once daily (N = 2829) or bicalutamide 50 mg orally once daily (N = 387). In these 8 trials, the median duration of treatment was 22.1 months (range: < 0.1 to 95.0) in patients that received XTANDI.

Seizure

Warning & Precaution

- Seizure occurred in 0.6% of patients receiving XTANDI in eight 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

Consider the Following in Discussing XTANDI With Patients:

- Inform patients that XTANDI has been associated with an increased risk of seizure
- Discuss conditions that may predispose to seizures and medications that may lower the seizure threshold
- Advise patients of the risk of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others
- Inform patients to contact their healthcare provider right away if they have loss of consciousness or seizure

Posterior Reversible Encephalopathy Syndrome (PRES)

Warning & Precaution

- 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

Consider the Following in Discussing XTANDI With Patients:

- Inform patients to contact their healthcare provider right away if they experience rapidly worsening symptoms possibly indicative of PRES such as seizure, headache, decreased alertness, confusion, reduced eyesight, or blurred vision

Patient Counseling Information[1]* (cont'd)

The information contained in this brochure does not constitute medical advice and is not intended to replace a healthcare provider's independent medical judgment regarding treatment management of individual patients

*The data in WARNINGS and PRECAUTIONS reflect 8 randomized, controlled trials [AFFIRM, PREVAIL, TERRAIN, PROSPER, ARCHES, EMBARK, Asian PREVAIL (NCT02294461), and STRIVE (NCT01664923)] that were pooled to conduct safety analyses in patients with CRPC (N = 3651), mCSPC (N = 752), or nmCSPC with high-risk BCR (n = 707) treated with XTANDI. Patients received XTANDI 160 mg (N = 5110) or placebo orally once daily (N = 2829) or bicalutamide 50 mg orally once daily (N = 387). In these 8 trials, the median duration of treatment was 22.1 months (range: < 0.1 to 95.0) in patients that received XTANDI.

Hypersensitivity

Warning & Precaution

- Hypersensitivity reactions, including edema of the face (0.5%), tongue (0.1%), or lip (0.1%) have been observed with XTANDI in eight 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

Consider the Following in Discussing XTANDI With Patients:

- Inform patients that XTANDI may be associated with hypersensitivity reactions that include swelling of the face, lip, tongue, or throat
- Advise patients who experience these types of symptoms of hypersensitivity to temporarily discontinue XTANDI and promptly contact their healthcare provider

Ischemic Heart Disease

Warning & Precaution

- In the combined data of five randomized, placebo-controlled clinical studies, ischemic heart disease occurred more commonly in patients on the XTANDI arm compared to patients on the placebo arm (3.5% vs 2%)
- Grade 3-4 ischemic events occurred in 1.8% of patients on XTANDI versus 1.1% 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

Consider the Following in Discussing XTANDI With Patients:

- Inform patients that XTANDI has been associated with an increased risk of ischemic heart disease
- Advise patients to seek immediate medical attention if any symptoms suggestive of a cardiovascular event occur

Patient Counseling Information[1]* (cont'd)

The information contained in this brochure does not constitute medical advice and is not intended to replace a healthcare provider's independent medical judgment regarding treatment management of individual patients

*The data in WARNINGS and PRECAUTIONS reflect 8 randomized, controlled trials [AFFIRM, PREVAIL, TERRAIN, PROSPER, ARCHES, EMBARK, Asian PREVAIL (NCT02294461), and STRIVE (NCT01664923)] that were pooled to conduct safety analyses in patients with CRPC (N = 3651), mCSPC (N = 752), or nmCSPC with high-risk BCR (n = 707) treated with XTANDI. Patients received XTANDI 160 mg (N = 5110) or placebo orally once daily (N = 2829) or bicalutamide 50 mg orally once daily (N = 387). In these 8 trials, the median duration of treatment was 22.1 months (range: < 0.1 to 95.0) in patients that received XTANDI.

Falls and Fractures

Warning & Precaution

- 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 five randomized, placebo-controlled clinical studies, falls occurred in 12% of patients treated with XTANDI compared to 6% of patients treated with placebo. Fractures occurred in 13% of patients treated with XTANDI and in 6% of patients treated with placebo

Consider the Following in Discussing XTANDI With Patients:

- Inform patients that XTANDI is associated with an increased incidence of dizziness/vertigo, falls, and fractures
- Advise patients to report these adverse reactions to their healthcare provider

Embryo-Fetal Toxicity

Warning & Precaution

- 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

Consider the Following in Discussing XTANDI With Patients:

- Inform patients that XTANDI can be harmful to a developing fetus and can cause loss of pregnancy
- 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
- Advise male patients to use a condom if having sex with a pregnant woman

Patient Counseling Information[1]* (cont'd)

The information contained in this brochure does not constitute medical advice and is not intended to replace a healthcare provider's independent medical judgment regarding treatment management of individual patients

*The data in WARNINGS and PRECAUTIONS reflect 8 randomized, controlled trials [AFFIRM, PREVAIL, TERRAIN, PROSPER, ARCHES, EMBARK, Asian PREVAIL (NCT02294461), and STRIVE (NCT01664923)] that were pooled to conduct safety analyses in patients with CRPC (N = 3651), mCSPC (N = 752), or nmCSPC with high-risk BCR (n = 707) treated with XTANDI. Patients received XTANDI 160 mg (N = 5110) or placebo orally once daily (N = 2829) or bicalutamide 50 mg orally once daily (N = 387). In these 8 trials, the median duration of treatment was 22.1 months (range: < 0.1 to 95.0) in patients that received XTANDI.

Hypertension

- In the combined data from five randomized placebo-controlled clinical trials, hypertension was reported in 14% of patients receiving XTANDI and 7% of patients receiving placebo
- Medical history of hypertension was balanced between arms
- Hypertension led to study discontinuation in < 1% of patients in each arm

Consider the Following in Discussing XTANDI With Patients:

- Inform patients that XTANDI is associated with an increased incidence of hypertension

Infertility

- Based on animal studies, XTANDI may impair fertility in males of reproductive potential

Consider the Following in Discussing XTANDI With Patients:

- Inform male patients that XTANDI may impair fertility

Reference

1. XTANDI [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

Clinical Trial Experience

In the data from the five randomized placebo-controlled trials, the most common ARs (≥ 10%) that occurred more frequently (≥ 2% over placebo) in XTANDI-treated patients were musculoskeletal pain, fatigue, hot flush, constipation, decreased appetite, diarrhea, hypertension, hemorrhage, fall, fracture, and headache. 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.[1]

AFFIRM: XTANDI + GnRH therapy* vs Placebo + GnRH therapy* in Metastatic CRPC Following Chemotherapy[1]

Eligibility criteria included[2,3]:

Patients who have progressed to mCRPC, were previously treated with 1 or 2 prior chemotherapy regimens (at least 1 of which was docetaxel-based), and had an ECOG status 0-2.†

Exclusion criteria included[1,2]:

Patients with a previous history of seizure, taking medicines known to decrease the seizure threshold, other risk factors for seizure, or clinically significant cardiovascular disease.

Randomized (N=1199) **2:1[1]**

- **XTANDI 160 mg/day + GnRH therapy[1]*** (n=800)
- **Placebo + GnRH therapy[1]*** (n=399)

Study treatment continued until disease progression (evidence of radiographic progression, a skeletal-related event, or clinical progression), initiation of new systemic antineoplastic treatment, unacceptable toxicity, or withdrawal.[1]

Primary endpoint[1]

- Overall survival

Safety Data

- The **most common all-grade ARs** that occurred in ≥ **20%** of XTANDI-treated patients were **asthenic conditions** (51% vs 44% placebo), **back pain** (26% vs 24% placebo), **diarrhea** (22% vs 18% placebo), **arthralgia** (21% vs 17% placebo), and **hot flush** (20% vs 10% placebo)[1]
- **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**[1]
- The **most common AR leading to treatment discontinuation** was **seizure**, which occurred in **0.9% of the XTANDI-treated patients** compared to **none (0%) of the placebo-treated patients**[1]

For more information on the AFFIRM trial, visit XtandiHCP.com

ECOG, Eastern Cooperative Oncology Group; **GnRH**, gonadotropin-releasing hormone; **mCRPC**, metastatic castration-resistant prostate cancer; **PSA**, prostate-specific antigen.

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

†92% of study participants had an ECOG Performance Status score of 0 or 1.[1] ECOG Performance Status scores range from 0 to 5, with 0 indicating full activity and 1 indicating a restriction in strenuous activity but the ability to be ambulatory and do light work.[4]

Clinical Trial Experience (cont'd)

PREVAIL: XTANDI + GnRH therapy* vs Placebo + GnRH therapy* in Chemotherapy-naive Metastatic CRPC[1]

Eligibility criteria included[5]:

- mCRPC
- Disease progression despite receiving GnRH therapy or after bilateral orchiectomy
- GnRH therapy* maintained
- Chemotherapy-naive
- Asymptomatic or mildly symptomatic

Exclusion criteria included[1,2,6]:

Prior abiraterone acetate use; history of seizure or a condition that might predispose to seizure, moderate or severe pain from prostate cancer, underlying brain injury with loss of consciousness, transient ischemic attack within the past 12 months and brain metastases; ECOG Performance Status ≥ 2; clinically significant cardiovascular disease.

Allowed[1,6]:

- Prior anti-androgen treatment
- Concomitant corticosteroid use
- Concomitant sipuleucel-T treatment
- Concomitant bisphosphonate or denosumab use
- Palliative radiation therapy
- Medications known to lower the seizure threshold
- Presence of visceral metastases
- History of mild to moderate heart failure

Randomized[1] (N=1717) **1:1**

- **XTANDI 160 mg/day + GnRH therapy[1]*** (n=872)
- **Placebo + GnRH therapy[1]*** (n=845)

Study treatment continued until disease progression (evidence of radiographic progression, a skeletal-related event, or clinical progression) and the initiation of a cytotoxic chemotherapy or an investigational agent, unacceptable toxicity, or withdrawal.[1]

Co-primary endpoints[1]

- Radiographic progression-free survival
  - Radiographic progression was assessed by BICR
- Overall survival

Safety Data

- **The most common all-grade ARs** that occurred in ≥ **20%** of XTANDI-treated patients were **asthenic conditions** (47% vs 33% in placebo), **back pain** (29% vs 22% in placebo), **constipation** (23% vs 17% placebo), and **arthralgia** (21% vs 16% in placebo)[1]
- **Grade 3-4 ARs** were reported in **44% of XTANDI-treated patients** and **37% of placebo-treated patients**. **Discontinuations due to AEs** were reported for **6% of XTANDI-treated patients**[1]
- The **most common AR leading to treatment discontinuation** was **fatigue/asthenia**, which occurred in 1% of patients on each treatment arm[1]

For more information on the PREVAIL trial, visit XtandiHCP.com

BICR, blinded independent central review; **BTA**, bone-targeting agent; **ECOG**, Eastern Cooperative Oncology Group; **GnRH**, gonadotropin-releasing hormone; **mCRPC**, metastatic castration-resistant prostate cancer; **PSA**, prostate-specific antigen; **RECIST 1.1**, Response Evaluation Criteria in Solid Tumors version 1.1.

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

Clinical Trial Experience (cont'd)

TERRAIN: XTANDI + GnRH therapy* vs Bicalutamide + GnRH therapy* in Chemotherapy-naive Metastatic CRPC[1]

Eligibility criteria included[1,7]:

- Metastatic disease despite receiving GnRH therapy*†
- Asymptomatic or mildly symptomatic prostate disease
- Not using opiate analgesics for prostate cancer–related pain
- GnRH therapy (or prior bilateral orchiectomy) maintained

Exclusion criteria included[1,7]:

- Prior progression on anti-androgen therapy
- Prior chemotherapy
- Brain metastasis
- History of seizure or a condition that might predispose to seizure
- Clinically significant cardiovascular disease
- Moderate to severe pain from prostate cancer

Allowed[7]:

- No age restrictions

Randomized[1] (N=375) **1:1**

- **XTANDI 160 mg/day + GnRH therapy[1]*** (n=184)
- **Bicalutamide 50 mg/day + GnRH therapy[1]*** (n=191)

Study treatment continued until disease progression (evidence of radiographic progression, a skeletal-related event), the initiation of subsequent antineoplastic agent, unacceptable toxicity, or withdrawal.[1]

Primary endpoint[1,7]

- Progression-free survival (ICR assessed)‡

Safety Data

- The **most common all-grade AR** that occurred in ≥ **20%** of XTANDI-treated patients was **asthenic conditions** (32% vs 23% bicalutamide)[1]
- **Grade 3-4 ARs** were reported in **39% of XTANDI-treated patients** and **38% of bicalutamide-treated patients**. **Discontinuations with an AE** as the primary reason were reported for **8% of XTANDI-treated patients** and **6% of bicalutamide-treated patients**[1]
- The **most common ARs leading to treatment discontinuation** were **back pain** and **pathological fracture**, which occurred in **3.8% of XTANDI-treated patients** for each event and in **2.1% and 1.6% of bicalutamide-treated patients**, respectively[1]

For more information on the TERRAIN trial, visit XtandiHCP.com

GnRH, gonadotropin-releasing hormone; **ICR**, Independent Central Review; **mCRPC**, metastatic castration-resistant prostate cancer; **PCWG2**, Prostate Cancer Clinical Trials Working Group 2; **PSA**, prostate-specific antigen; **RECIST 1.1**, Response Evaluation Criteria in Solid Tumors version 1.1.

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

†Disease progression was defined as the presence of 1 or more of the following 3 criteria: 1) PSA progression (≥ 3 measurements of rising PSA concentrations with an interval of at least 1 week between determinations); 2) soft-tissue disease progression defined by RECIST 1.1; 3) bone disease progression defined by at least 2 new lesions on bone scan.[7]

‡Progression-free survival was defined as the time from randomization to the first progression event, which includes radiographic disease progression, skeletal-related event, initiation of a new antineoplastic therapy, and death.[7]

Clinical Trial Experience (cont'd)

PROSPER: XTANDI + GnRH therapy* vs Placebo + GnRH therapy* in Non-metastatic CRPC Patients[1]

Eligibility criteria included[8,9]:

nmCRPC (central review), ≥ 3 rising PSA values despite castrate testosterone levels (≤ 50 ng/dL),† baseline PSA ≥ 2 ng/mL, PSADT ≤ 10 months, no prior chemotherapy, and ECOG performance status of 0 or 1.

Exclusion criteria included[9]:

Prior abiraterone acetate use, history of seizure, underlying brain injury with loss of consciousness, transient ischemic attack within the past 12 months, or clinically significant cardiovascular disease.

Permitted at baseline[1,2]:

- Prior anti-androgen therapy with a 4-week washout period prior to randomization
- Bicalutamide treatment prior to randomization was received by 56% of patients

Stratification factors[1,2]:

- PSADT (< 6 months or ≥ 6 months)
- Baseline use of BTA (yes or no)

Randomized[1] (N=1401) **2:1**

- **XTANDI 160 mg/day + GnRH therapy[1]*** (n=933)
- **Placebo + GnRH therapy[1]*** (n=468)

Treatment continued until radiographic disease progression† confirmed by blinded independent central review, initiation of new treatment, unacceptable toxicity, or withdrawal. PSA results were blinded and were not used for treatment discontinuation.[1]

Primary endpoint[1]

- Metastasis-free survival

Safety Data

- The **most common all-grade AR** that occurred in ≥ **20%** of XTANDI-treated patients was **asthenic conditions** (40% vs 20% placebo)[1]
- **Grade 3 or higher ARs** were reported in **31% of XTANDI-treated patients** and **23% of placebo-treated patients**. **Discontinuations with an AE** as the primary reason were reported for **9% of XTANDI-treated patients** and **6% of placebo-treated patients**[1]
- The **most common AE leading to treatment discontinuation** was **fatigue**, which occurred in **1.6% of the XTANDI-treated patients** compared to **none of the placebo-treated patients**[1]
- Overall, 32 patients **(3.4%) receiving XTANDI died from AEs**. Three patients **(0.6%) receiving placebo died from AEs**[1]

For more information on the PROSPER trial, visit XtandiHCP.com

BTA, bone-targeting agent; **ECOG**, Eastern Cooperative Oncology Group; **GnRH**, gonadotropin-releasing hormone; **nmCRPC**, nonmetastatic castration-resistant prostate cancer; **PSA**, prostate-specific antigen; **PSADT**, prostate-specific antigen doubling time.

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

†Progression was defined as at least 3 rising PSA values (PSA1 < PSA2 < PSA3) taken at least 1 week apart despite castrate levels of testosterone (≤ 50 ng/dL) on GnRH therapy or after bilateral orchiectomy.[8]

Clinical Trial Experience (cont'd)

ARCHES: XTANDI + GnRH therapy* vs Placebo + GnRH therapy* in Metastatic CSPC Patients[1]

Eligibility criteria included[10]:
Pathologically confirmed adenocarcinoma of the prostate; metastatic prostate cancer, either de novo or after recurrence after prior local therapy, documented by positive bone scan or metastatic lesions on CT or MRI scan; ECOG performance status 0 or 1.

Exclusion criteria included[11]:
Within 4 weeks of baseline, receipt of major surgery, investigational agent, or treatment with therapies thought to affect androgen synthesis or PSA levels; known or suspected brain metastasis; history of seizure or any condition that may predispose to seizure; within 12 months of baseline, history of loss of consciousness or transient ischemic attack, experience of clinically significant cardiovascular disease.

Permitted at baseline[2]:
- ≤ 3 months of GnRH therapy if docetaxel-naive; ≤ 6 months of GnRH therapy if docetaxel-experienced
- 1 course of metastasis-targeted palliative radiation or surgery
- ≤ 6 cycles of prior docetaxel therapy

Stratification factors[1]:
- Volume of disease (low vs high†)
- Prior docetaxel therapy for prostate cancer (none, 1 to 5, or 6 cycles)

Randomized[1] (N=1150) **1:1**

- **XTANDI 160 mg/day + GnRH therapy[1]*** (n=574)
- **Placebo + GnRH therapy[1]*** (n=576)

Treatment continued until radiographic disease progression‡ (confirmed by blinded independent central review), initiation of new treatment, unacceptable toxicity, or withdrawal.[1]

Primary endpoint[1]

- Radiographic progression-free survival§

Safety Data

- The **most common all-grade ARs** that occurred in ≥ **20%** of XTANDI-treated patients were **asthenic conditions** (24% vs 20% in placebo) and **hot flush** (27% vs 22% placebo)[1]
- **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 **4.9% of XTANDI-treated patients** and **3.7% of placebo-treated patients**[1]
- The most common AEs resulting in permanent discontinuation in XTANDI-treated patients were **alanine aminotransferase increased**, **aspartate aminotransferase elevation**, and **seizure**, each in **0.3%**. The most common AEs leading to permanent discontinuation in placebo-treated patients were **arthralgia** and **fatigue**, each in **0.3%**[1]
- Overall, 10 patients **(1.7%) receiving XTANDI died from AEs**. Eight patients **(1.4%) receiving placebo died from AEs**[1]

For more information on the ARCHES trial, visit XtandiHCP.com

CT, computed tomography; **ECOG**, Eastern Cooperative Oncology Group; **GnRH**, gonadotropin-releasing hormone; **MRI**, magnetic resonance imaging; **PSA**, prostate-specific antigen.
***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.[10]
‡Radiographic disease progression was defined by identification of ≥ 2 new bone lesions on a bone scan with confirmation (Prostate Cancer Working Group 2 criteria) and/or progression in soft-tissue disease.[1]
§Radiographic progression-free survival was defined as the time from randomization to radiographic disease progression at any time or death within 24 weeks after study drug discontinuation.[10]

Clinical Trial Experience (cont'd)

EMBARK: XTANDI with or without GnRH therapy* vs placebo + GnRH therapy* in nmCSPC with high-risk BCR[1]

Patient population[1,12]: All patients had prior definitive therapy with RP or RT (including brachytherapy) with curative intent, or both; confirmation of nonmetastatic disease by BICR; screening PSA ≥ 1 ng/mL after RP (with or without RT) as the primary treatment for prostate cancer or at least 2 ng/mL above the nadir after prior RT only; PSA doubling time ≤ 9 months; testosterone ≥ 150 ng/dL; ECOG Performance Status 0-1 at screening.

Exclusion criteria (select)[13]: Prior/current distant metastasis; prior hormonal therapy generally not allowed except for short courses ≤ 36 months in duration and ≥ 9 months before randomization; suitable candidate for salvage RT if prior prostatectomy; prior cytotoxic chemotherapy/systemic biologic therapy, including immunotherapy, for prostate cancer; history of seizure or any seizure-predisposing condition; and clinically significant cardiovascular disease.

Patients were offered a treatment suspension once at Week 37 if PSA was < 0.2 ng/mL at Week 36; treatment was reinitiated when PSA values increased to ≥ 2.0 ng/mL for patients with prior prostatectomy or ≥ 5.0 ng/mL for patients without prior prostatectomy. All treatment arms were eligible for treatment suspension. In the XTANDI + GnRH therapy* and placebo + GnRH therapy* arms, GnRH therapy* was also suspended.[1]

Stratification factors[1]: Screening PSA (≤ 10 ng/mL vs > 10 ng/mL); PSA doubling time (≤ 3 months vs > 3 months to ≤ 9 months); prior hormonal therapy.

Randomized[1] (N = 1068) **1:1:1**

Primary

- **XTANDI** (160 mg/day) **+ GnRH therapy*** (n = 355)[1] (double blind)[13]
- Placebo + GnRH therapy* (n = 358)[1] (double blind)[13]

Secondary

- **XTANDI** (single agent) (160 mg/day) (n = 355)[1] (open label)[1]

Treatment† was suspended if PSA dropped to < 0.2 ng/mL at 36 weeks[1]

Week 37

PSA < 0.2 ng/mL at Week 36

Yes → Treatment was suspended at Week 37 and PSA was monitored (treatment was reinitiated when PSA increased)‡. 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.

No → Treatment continued

Treatment was permanently discontinued upon radiographic disease progression confirmed by BICR, initiation of new treatment, unacceptable toxicity, or withdrawal.[1]

In the EMBARK trial, patients were required to have nonmetastatic disease by BICR, high-risk BCR (defined by a PSA doubling time ≤ 9 months), and PSA values ≥ 1 ng/mL if they had prior RP (with or without RT) as the primary treatment for prostate cancer or PSA values ≥ 2 ng/mL above the nadir if they had prior RT only.[1]
BCR, biochemical recurrence; **BICR**, blinded independent central review; **ECOG**, Eastern Cooperative Oncology Group; **GnRH**, gonadotropin-releasing hormone; **PSA**, prostate-specific antigen; **RP**, radical prostatectomy; **RT**, radiotherapy.
***Leuprolide.[1]**
†All treatment arms were eligible for treatment suspension. In the XTANDI + GnRH therapy* and placebo + GnRH therapy* arms, GnRH therapy* was also suspended.[1]
‡Study treatment was suspended once at Week 37 if PSA was < 0.2 ng/mL at Week 36; treatment was reinitiated when PSA values increased to ≥ 2.0 ng/mL for patients with prior prostatectomy or ≥ 5.0 ng/mL for patients without prior prostatectomy.[1]

Clinical Trial Experience (cont'd)

EMBARK: XTANDI with or without GnRH therapy* vs placebo + GnRH therapy* in nmCSPC with high-risk BCR[1]

Primary endpoint[1]

- Metastasis-free survival (XTANDI + GnRH therapy* vs placebo + GnRH therapy*)

Safety Data

- **The most common all-grade ARs** that occurred in ≥ **20%** of patients receiving XTANDI + GnRH therapy*, XTANDI as a single agent, or placebo + GnRH therapy*, respectively, were **hot flush** (69%, 22%, and 57%), **fatigue** (50%, 54%, and 38%), **musculoskeletal pain** (50%, 48%, and 43%), **fall** (21%, 16%, and 14%), **hemorrhage** (20%, 21%, and 15%), **gynecomastia** (9%, 49%, and 10%), and **breast tenderness** (5%, 35%, and 2.8%)[1]
- **Grade 3 or higher ARs** were reported in **46% of patients receiving XTANDI + GnRH therapy*, 50% of patients receiving XTANDI as a single agent**, and 43% of patients receiving placebo + GnRH therapy*. **Discontinuations with an AE** as the primary reason were reported for **21% of patients receiving XTANDI + GnRH therapy*, 18% of patients receiving XTANDI as a single agent**, and **10% of patients receiving placebo + GnRH therapy***[1]
- **The most common ARs resulting in permanent discontinuation** included **fatigue (3.4% of patients receiving XTANDI + GnRH therapy*, 3.7% of patients receiving XTANDI as a single agent**, and **1.4% of patients receiving placebo + GnRH therapy*), hot flush (2% of patients treated with XTANDI + GnRH therapy*, 0% of patients receiving XTANDI as a single agent**, and **1.1% of patients receiving placebo + GnRH therapy*), nausea (1.1% of patients treated with XTANDI + GnRH therapy*, 0.6% of patients receiving XTANDI as a single agent**, and **0.3% of patients receiving placebo + GnRH therapy*), and cognitive disorder (1.1% of patients treated with XTANDI + GnRH therapy*, 1.4% of patients receiving XTANDI as a single agent**, and **0.8% of patients receiving placebo + GnRH therapy*)**[1]
- Overall, 6 patients **(1.7%) receiving XTANDI + GnRH therapy***, 8 patients **(2.3%) receiving XTANDI as a single agent**, and 3 patients **(0.8%) receiving placebo + GnRH therapy*** **died from ARs**[1]

For more information on the EMBARK trial, visit XtandiHCP.com

***Leuprolide.[1]**

Post-Marketing Experience[1]*

The following additional adverse reactions have been identified during post-approval use of XTANDI:

- **Gastrointestinal Disorders:** vomiting
- **Immune System Disorders:** hypersensitivity (edema of the face, tongue, lip, or pharynx)
- **Neurological Disorders:** PRES, dysgeusia
- **Skin and Subcutaneous Tissue Disorders:** rash, severe cutaneous adverse reactions (including Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, and acute generalized exanthematous pustulosis)

*Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Important Safety Information
Adverse Reactions (ARs)

In the data from the five randomized placebo-controlled trials, the most common ARs (≥ 10%) that occurred more frequently (≥ 2% over placebo) in XTANDI-treated patients were musculoskeletal pain, fatigue, hot flush, constipation, decreased appetite, diarrhea, hypertension, hemorrhage, fall, fracture, and headache. 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 ARs 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 ARs 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 AR as the primary reason were reported for 8% of XTANDI patients and 6% of bicalutamide patients.

References

1. XTANDI [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** Data on file. XTANDI. Pfizer Inc., New York, NY. **3.** Protocol for: 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. **4.** 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. **5.** Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med 2014;371(5):424-33. **6.** Protocol for: Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med 2014;371(5):424-33. **7.** Shore ND, Chowdhury S, Villers A, et al. Efficacy and safety of enzalutamide versus bicalutamide for patients with metastatic prostate cancer (TERRAIN): a randomised, double-blind, phase 2 study. Lancet Oncol 2016;17(2):153-63. **8.** Hussain M, Fizazi K, Saad F, et al. Enzalutamide in men with nonmetastatic, castration-resistant prostate cancer. N Engl J Med 2018;378(26):2465-74. **9.** Protocol for: Hussain M, Fizazi K, Saad F, et al. Enzalutamide in men with nonmetastatic, castration-resistant prostate cancer. N Engl J Med 2018;378(26):2465-74. **10.** 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. **11.** Protocol for: 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. **12.** Freedland SJ, de Almeida Luz M, De Giorgi U, et al. Improved outcomes with enzalutamide in biochemically recurrent prostate cancer. N Engl J Med 2023;389(16):1453-65. **13.** Freedland SJ, De Giorgi U, Gleave M, et al. A phase 3 randomised study of enzalutamide plus leuprolide and enzalutamide monotherapy in high-risk non-metastatic hormone-sensitive prostate cancer with rising PSA after local therapy: EMBARK study design. BMJ Open (Epub) 08-12-2021.

Information for Counseling Patients About Certain Adverse Reactions

These tips come from organizations, including those that support people with cancer; they have not been studied with XTANDI.

Fatigue

Diet[1]

- Consider talking with patients about how to maintain adequate hydration and nutrition

Physical Activity[1,2]

- Consider talking with patients about how exercise can contribute to both physical and mental health
- **Patients should speak to their healthcare team first before starting any physical activity routine**

Concomitant Medications Contributing to Fatigue[1]

- Consider if the coadministration of multiple drugs with varying side effects may compound fatigue symptoms

Focus on Relaxing[1]

- Consider talking with patients about attention-restoring activities, such as walking and gardening
- Patients could schedule important daily activities during times of least fatigue and eliminate nonessential, stress-producing activities

Sleep Hygiene[3,4]

- An assessment of sleep hygiene and use of behavioral management strategies may reduce sleep disturbances
- Areas in which patients could modify their sleep routines include:
  - Having regular times to go to bed and get up in the morning
  - Avoiding exercising too late in the evening
  - Napping, if needed, for less than 30 minutes and early in the day so that nighttime sleep is not impacted

The information contained in this brochure does not constitute medical advice and is not intended to replace a healthcare provider's independent medical judgment regarding treatment management of individual patients

Important Safety Information
Adverse Reactions (ARs)

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

References

1. National Cancer Institute. Fatigue (PDQ®)–health professional version (09-01-2022). https://www.cancer.gov/about-cancer/treatment/side-effects/fatigue/fatigue-hp-pdq. Accessed 10-21-2022. **2.** American Society of Clinical Oncology. Exercise during cancer treatment (06-2022). https://www.cancer.net/survivorship/healthy-living/exercise-during-cancer-treatment. Accessed 03-08-2023. **3.** National Cancer Institute. Sleep Disorders (PDQ®)–health professional version (02-21-2023). https://www.cancer.gov/about-cancer/treatment/side-effects/sleep-disorders-hp-pdq. Accessed 04-20-2023. **4.** American Cancer Society. Getting help for fatigue (04-2020). https://www.cancer.org/content/dam/cancer-org/cancer-control/en/booklets-flyers/getting-help-for-fatigue.pdf. Accessed 01-31-2023.

Information for Counseling Patients About Certain Adverse Reactions (cont'd)

These tips come from organizations, including those that support people with cancer; they have not been studied with XTANDI.

Falls

Physical Activity[1,2]

- Patients may participate in activities designed to improve balance and strength as a fall prevention strategy. Common exercises recommended to reduce the risk of falls include Tai Chi, balance classes, and strength exercises that patients can practice at home
- **Patients should speak to their healthcare team first before starting any physical activity routine**

Concomitant Medications Contributing to Fall Risk[3]

- Consider a medication review with patients 65 years and older to identify prescription drugs, over-the-counter medications, and herbal supplements that could potentially increase their fall risk

Home Organization[1,4]

- Patients may need to modify their home environment to minimize fall hazards, such as by:
  - Adding grab bars in bathrooms, especially in the shower and bathtub due to slippery floors
  - Removing throw rugs from the floors

The information contained in this brochure does not constitute medical advice and is not intended to replace a healthcare provider's independent medical judgment regarding treatment management of individual patients

Important Safety Information
Adverse Reactions (ARs)

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

In EMBARK, the placebo-controlled study of nonmetastatic CSPC (nmCSPC) with high-risk biochemical recurrence (BCR) patients, Grade 3 or higher adverse reactions during the total duration of treatment were reported in 46% of patients treated with XTANDI plus leuprolide, 50% of patients receiving XTANDI as a single agent, and 43% of patients receiving placebo plus leuprolide. Permanent treatment discontinuation due to adverse reactions during the total duration of treatment as the primary reason was reported in 21% of patients treated with XTANDI plus leuprolide, 18% of patients receiving XTANDI as a single agent, and 10% of patients receiving placebo plus leuprolide.

References

1. Centers for Disease Control and Prevention. Fact sheet: talking about fall prevention with your patients (2017). https://www.cdc.gov/steadi/pdf/STEADI-FactSheet-TalkingWPatients-508.pdf. Accessed 03-23-2023. **2.** American Society of Clinical Oncology. Exercise during cancer treatment (06-2022). https://www.cancer.net/survivorship/healthy-living/exercise-during-cancer-treatment. Accessed 03-08-2023. **3.** Centers for Disease Control and Prevention. Fact sheet: medications linked to falls (2017). https://www.cdc.gov/steadi/pdf/STEADI-FactSheet-MedsLinkedtoFalls-508.pdf. Accessed 04-20-2023. **4.** Centers for Disease Control and Prevention. Preventing falls in older patients: provider pocket guide (2019). https://www.cdc.gov/steadi/pdf/STEADI-PocketGuide-508.pdf. Accessed 04-20-2023.

Information for Counseling Patients About Certain Adverse Reactions (cont'd)

These tips come from organizations, including those that support people with cancer; they have not been studied with XTANDI.

Fractures

Patient Evaluation for Fracture Risk[1]

- Consider evaluating patients for fracture and fall risk

Use of Bone-Targeted Agents[1]

- Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents

Physical Activity[2]

- Patients may take part in exercise routines including the following elements:
  - Strength training
  - Resistance training
- **Patients should speak to their healthcare team first before starting any physical activity routine**

The information contained in this brochure does not constitute medical advice and is not intended to replace a healthcare provider's independent medical judgment regarding treatment management of individual patients

Important Safety Information
Adverse Reactions (ARs)

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 hemoglobin decrease, neutrophil count decreased, white blood cell decreased, hyperglycemia, hypermagnesemia, hyponatremia, hyperphosphatemia, and hypercalcemia.

References

1. XTANDI [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** American Society of Clinical Oncology. Exercise during cancer treatment (06-2022). https://www.cancer.net/survivorship/healthy-living/exercise-during-cancer-treatment. Accessed 03-08-2023.

Information for Counseling Patients About Certain Adverse Reactions (cont'd)

These tips come from organizations, including those that support people with cancer; they have not been studied with XTANDI.

Hot Flush

Lowering Body Temperature[1]

- Patients could try to reduce the frequency or intensity of flushes by:
  - Wearing materials made of natural instead of artificial fibers (e.g., silk and cotton)
  - Dressing in layers of clothing to be able to easily remove clothes if overheated
  - Taking showers with lukewarm water and using cooling pads
  - Maintaining a cooler environment, using a fan if necessary
  - Sipping cold or iced drinks

Dietary and Lifestyle Modifications[1]

- As certain substance use and food intake can increase the frequency or intensity of hot flushes, patients may consider the following non-pharmacologic lifestyle modifications:
  - Cut out or reduce alcohol and caffeinated drinks
  - Reduce or stop smoking and the use of any nicotine-based products
  - Cut out or reduce spicy foods from the diet

Stress Management[2]

- Since serotonin may be involved as a central hot flush trigger, behavioral interventions such as stress management may modulate serotonin, causing a decrease in hot flushes

The information contained in this brochure does not constitute medical advice and is not intended to replace a healthcare provider's independent medical judgment regarding treatment management of individual patients

Important Safety Information
Adverse Reactions (ARs)

Hypertension: In the combined data from five randomized placebo-controlled clinical trials, hypertension was reported in 14.2% of XTANDI patients and 7.4% 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.

Please see Important Safety Information throughout. Please see Full Prescribing Information and Patient Handout Card in the pocket.

References

1. Cancer Research UK. Hot flushes in men (10-06-2022). https://www.cancerresearchuk.org/about-cancer/prostate-cancer/practical-emotional-support/hormone-symptoms/sex-hormones-hot-flushes. Accessed 03-08-2023. **2.** National Cancer Institute. Hot Flashes and Night Sweats (PDQ®)–health professional version (10-19-2022). https://www.cancer.gov/about-cancer/treatment/side-effects/hot-flashes-hp-pdq. Accessed 04-20-2023.

Patient Handout Cards

Please give your patient the handout card to help with tools, tips, and patient support.

© 2024 Astellas Pharma US, Inc. and Pfizer Inc. All rights reserved. 076-9220-PM 02/24
XTANDI, Astellas, and the flying star logo are registered trademarks of Astellas Pharma Inc.