

DOSING AND ADMINISTRATION



ERLEADA[®] offers once-daily oral dosing¹



Tablets shown are not actual size.

The recommended dose of ERLEADA[®] is 240 mg (four 60 mg tablets) administered

ORALLY ONCE DAILY¹

Patients should also receive a GnRH analog concurrently or should have had a bilateral orchiectomy.¹



No need for co-administration of corticosteroid.¹



Can be taken with or without food. Tablets should be swallowed whole.¹



No initial dose adjustments for ERLEADA[®] are necessary for mild to moderate renal or hepatic impairment.¹ ERLEADA[®] has not been evaluated in patients with severe renal or hepatic impairment.

Dose modifications

- If a patient experiences a \geq Grade 3 toxicity or an intolerable side effect, hold dosing until symptoms improve to \leq Grade 1 or original grade, and then resume at the same dose or a reduced dose (180 mg or 120 mg), if warranted¹

GnRH = gonadotropin-releasing hormone.

INDICATION

ERLEADA[®] (apalutamide) is an androgen receptor inhibitor indicated for the treatment of patients with:

- Metastatic castration-sensitive prostate cancer (mCSPC)
- Non-metastatic castration-resistant prostate cancer (nmCRPC)

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Cerebrovascular and Ischemic Cardiovascular Events — In a randomized study (SPARTAN) of patients with nmCRPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA[®] and 3% of patients treated with placebo. In a randomized study (TITAN) in patients with mCSPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA[®] and 2% of patients treated with placebo. Across the SPARTAN and TITAN studies, 5 patients (0.5%) treated with ERLEADA[®] and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event.

Learn about an alternate way to take ERLEADA[®]

- For patients who have difficulty swallowing tablets, ERLEADA[®] may be taken by mixing the tablets in applesauce. Please see Section 2.3 of the full [Prescribing Information](#) for ERLEADA[®] to learn more about this alternate method of administration

Patients with history of unstable angina, myocardial infarction, congestive heart failure, stroke, or transient ischemic attack within 6 months of randomization were excluded from the SPARTAN and TITAN studies.

In the SPARTAN study, cerebrovascular events occurred in 4.7% of patients treated with ERLEADA[®] and 0.8% of patients treated with placebo. In the TITAN study, cerebrovascular events occurred in 1.9% of patients treated with ERLEADA[®] and 2.1% of patients treated with placebo. Across the SPARTAN and TITAN studies, 3 patients (0.2%) treated with ERLEADA[®], and 2 patients (0.2%) treated with placebo died from a cerebrovascular event.

Cerebrovascular and ischemic cardiovascular events, including events leading to death, occurred in patients receiving ERLEADA[®]. Monitor for signs and symptoms of ischemic heart disease and cerebrovascular disorders. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Consider discontinuation of ERLEADA[®] for Grade 3 and 4 events.

Please see [page 2](#) for additional Important Safety Information that includes information about drug interactions and see the full [Prescribing Information](#) for ERLEADA[®].

IMPORTANT SAFETY INFORMATION (continued)

Fractures — In a randomized study (SPARTAN) of patients with nmCRPC, fractures occurred in 12% of patients treated with ERLEADA[®] and in 7% of patients treated with placebo. In a randomized study (TITAN) of patients with mCSPC, fractures occurred in 9% of patients treated with ERLEADA[®] and in 6% of patients treated with placebo. Evaluate patients for fracture risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

Falls — In a randomized study (SPARTAN), falls occurred in 16% of patients treated with ERLEADA[®] compared with 9% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure. Falls occurred in patients receiving ERLEADA[®] with increased frequency in the elderly. Evaluate patients for fall risk.

Seizure — In two randomized studies (SPARTAN and TITAN), 5 patients (0.4%) treated with ERLEADA[®] and 1 patient treated with placebo (0.1%) experienced a seizure. Permanently discontinue ERLEADA[®] in patients who develop a seizure during treatment. It is unknown whether anti-epileptic medications will prevent seizures with ERLEADA[®]. Advise patients of the risk of developing a seizure while receiving ERLEADA[®] and of engaging in any activity where sudden loss of consciousness could cause harm to themselves or others.

Embryo-Fetal Toxicity — The safety and efficacy of ERLEADA[®] have not been established in females. Based on its mechanism of action, ERLEADA[®] 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 and for 3 months after the last dose of ERLEADA[®] [see *Use in Specific Populations* (8.1, 8.3)].

ADVERSE REACTIONS

Adverse Reactions — The most common adverse reactions (≥10%) that occurred more frequently in the ERLEADA[®]-treated patients (≥2% over placebo) from the randomized placebo-controlled clinical trials (TITAN and SPARTAN) were fatigue, arthralgia, rash, decreased appetite, fall, weight decreased, hypertension, hot flush, diarrhea, and fracture.

Laboratory Abnormalities — All Grades (Grade 3-4)

- **Hematology** — In the TITAN study: white blood cell decreased ERLEADA[®] 27% (0.4%), placebo 19% (0.6%); anemia ERLEADA[®] 70% (0.4%), placebo 64% (0.5%); leukopenia ERLEADA[®] 47% (0.3%), placebo 29% (0%); lymphopenia ERLEADA[®] 41% (2%), placebo 21% (2%)
- **Chemistry** — In the TITAN study: hypertriglyceridemia ERLEADA[®] 17% (3%), placebo 12% (2%); hypercholesterolemia ERLEADA[®] 76% (0.1%), placebo 46% (0%); hyperglycemia ERLEADA[®] 70% (2%), placebo 59% (1%); hypertriglyceridemia ERLEADA[®] 67% (2%), placebo 49% (0.8%); hyperkalemia ERLEADA[®] 32% (2%), placebo 22% (0.5%)

Rash — In 2 randomized studies (SPARTAN and TITAN), rash was most commonly described as macular or maculopapular. Adverse reactions of rash were 26% with ERLEADA[®] vs 8% with placebo. Grade 3 rashes (defined as covering >30% body surface area [BSA]) were reported with ERLEADA[®] treatment (6%) vs placebo (0.5%).

The onset of rash occurred at a median of 83 days. Rash resolved in 78% of patients within a median of 78 days from onset of rash. Rash was commonly managed with oral antihistamines, topical corticosteroids, and 19% of patients received systemic corticosteroids. Dose reduction or dose interruption occurred in 14% and 28% of patients, respectively. Of the patients who had dose interruption, 59% experienced recurrence of rash upon reintroduction of ERLEADA[®].

Hypothyroidism — In 2 randomized studies (SPARTAN and TITAN), hypothyroidism was reported for 8% of patients treated with ERLEADA[®] and 2% of patients treated with placebo based on assessments of thyroid-stimulating hormone (TSH) every 4 months. Elevated TSH occurred in 25% of patients treated with ERLEADA[®] and 7% of patients treated with placebo. The median onset was at the first scheduled assessment. There were no Grade 3 or 4 adverse reactions. Thyroid replacement therapy, when clinically indicated, should be initiated or dose-adjusted.

DRUG INTERACTIONS

Effect of Other Drugs on ERLEADA[®] — Co-administration of a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties. No initial dose adjustment is necessary; however, reduce the ERLEADA[®] dose based on tolerability [see *Dosage and Administration* (2.2)].

Effect of ERLEADA[®] on Other Drugs

CYP3A4, CYP2C9, CYP2C19, and UGT Substrates — ERLEADA[®] is a strong inducer of CYP3A4 and CYP2C19, and a weak inducer of CYP2C9 in humans. Concomitant use of ERLEADA[®] with medications that are primarily metabolized by CYP3A4, CYP2C19, or CYP2C9 can result in lower exposure to these medications. Substitution for these medications is recommended when possible or evaluate for loss of activity if medication is continued. Concomitant administration of ERLEADA[®] with medications that are substrates of UDP-glucuronosyl transferase (UGT) can result in decreased exposure. Use caution if substrates of UGT must be co-administered with ERLEADA[®] and evaluate for loss of activity.

P-gp, BCRP, or OATP1B1 Substrates — Apalutamide is a weak inducer of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), and organic anion transporting polypeptide 1B1 (OATP1B1) clinically. Concomitant use of ERLEADA[®] with medications that are substrates of P-gp, BCRP, or OATP1B1 can result in lower exposure of these medications. Use caution if substrates of P-gp, BCRP, or OATP1B1 must be co-administered with ERLEADA[®] and evaluate for loss of activity if medication is continued.

Please see the full **Prescribing Information** for ERLEADA[®].

Reference: 1. ERLEADA[®] [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.