Erleada® (apalutamide) 60 mg tablets 240 mg tablet

THE ONLY ANDROGEN RECEPTOR INHIBITOR WITH THE CONVENIENCE OF ALTERNATE METHODS OF ADMINISTRATION FOR PATIENTS WHO CANNOT SWALLOW TABLETS WHOLE OR HAVE A FEEDING TUBE [1-3]

ERLEADA® comes in 2 different strengths, 240 mg tablets and 60 mg tablets. Please find the instructions below that refer to each prescribed ERLEADA® strength.

HOW TO DISPERSE 240 MG TABLET IN WATER AND ADMINISTER WITH ORANGE JUICE, APPLESAUCE, OR ADDITIONAL WATER

For patients who cannot swallow tablets whole, the recommended dose of ERLEADA® tablet can be dispersed in noncarbonated water and then administered with either orange juice, applesauce, or additional noncarbonated water as follows:

Directions:

1. Place the whole ERLEADA® tablet in a cup. **Do not crush or split the tablet.**
2. Add about 2 teaspoons (10 mL) of noncarbonated water to make sure that the tablet is completely immersed in water.
3. Wait 2 minutes until the tablet is broken up and spread out, and then stir the mixture.
4. Add 2 tablespoons (30 mL) of either orange juice, applesauce, or additional noncarbonated water and stir the mixture.
5. Swallow the mixture immediately.
6. Rinse the cup with enough noncarbonated water to make sure the whole dose is taken, and drink it immediately.

Do not store ERLEADA® that is mixed with noncarbonated water, orange juice, or applesauce for later use.

HOW TO ADMINISTER ERLEADA® 240 MG TABLET THROUGH A FEEDING TUBE

ERLEADA® tablet can be administered through a feeding tube 8 French or greater as follows[1]:

1. Place the tablet in the barrel of the syringe (use at least a 20 mL syringe) and draw up 10 mL of noncarbonated water into the syringe.
2. Wait 10 minutes and then shake vigorously to disperse contents completely.
3. Administer immediately through the feeding tube.
4. Refill the syringe with noncarbonated water and administer. Repeat until no tablet residue is left in the syringe or feeding tube.

HOW TO DISPERSE 60 MG TABLETS IN WATER AND ADMINISTER WITH ORANGE JUICE, APPLESAUCE, OR ADDITIONAL WATER

For patients who cannot swallow tablets whole, the recommended dose of ERLEADA® 60 mg tablets can be dispersed in noncarbonated water and then administered with either orange juice, applesauce, or additional water as follows:

Directions:

1. Place the entire prescribed dose of ERLEADA® 60 mg tablets in a cup. **Do not crush or split the tablets.**
2. Add about 4 teaspoons (20 mL) of noncarbonated water to make sure that the tablets are completely immersed in water.
3. Wait 2 minutes until the tablets are broken up and spread out, and then stir the mixture.
4. Add 2 tablespoons (30 mL) of either orange juice, applesauce, or additional noncarbonated water and stir the mixture.
5. Swallow the mixture immediately.
6. Rinse the cup with enough water to make sure the whole dose is taken and drink it immediately.

Do not store ERLEADA® that is mixed with noncarbonated water, orange juice, or applesauce for later use.

HOW TO ADMINISTER ERLEADA® 60 MG TABLETS THROUGH A FEEDING TUBE

ERLEADA® tablets can be administered through a feeding tube 8 French or greater as follows[1]:

1. Place the entire prescribed dose of ERLEADA® tablets in the barrel of the syringe (use at least a 50 mL syringe) and draw up 20 mL of noncarbonated water into the syringe.
2. Wait 10 minutes and then shake vigorously to disperse contents completely.
3. Administer immediately through the feeding tube.
4. Refill the syringe with noncarbonated water and administer. Repeat until no tablet residue is left in the syringe or feeding tube.

References: 1. ERLEADA® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Nubeqa® [Prescribing Information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc. **3.** Xtandi® [Prescribing Information]. Northbrook, IL: Astellas Pharma US, Inc.

INDICATIONS

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 3.7% of patients treated with ERLEADA® and 2% of patients treated with placebo. In a randomized study (TITAN) in patients with mCSPC, ischemic cardiovascular events occurred in 4.4% of patients treated with ERLEADA® and 1.5% of patients treated with placebo. Across the SPARTAN and TITAN studies, 4 patients (0.3%) treated with ERLEADA® and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event. 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 2.5% of patients treated with ERLEADA® and 1% 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.

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 2 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.

Severe Cutaneous Adverse Reactions — Fatal and life-threatening cases of severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) occurred in patients receiving ERLEADA®.

Monitor patients for the development of SCARs. Advise patients of the signs and symptoms of SCARs (eg, a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash, or lymphadenopathy). If a SCAR is suspected, interrupt ERLEADA® until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended. If a SCAR is confirmed, or for other Grade 4 skin reactions, permanently discontinue ERLEADA® *[see Dosage and Administration (2.2)]*.

Interstitial Lung Disease (ILD)/Pneumonitis — Fatal and life-threatening interstitial lung disease (ILD) or pneumonitis can occur in patients treated with ERLEADA®.

Post-marketing cases of ILD/pneumonitis, including fatal cases, occurred in patients treated with ERLEADA®. Across clinical trials (TITAN and SPARTAN, n=1327), 0.8% of patients treated with ERLEADA® experienced ILD/pneumonitis, including 0.2% who experienced Grade 3 events *[see Adverse Reactions (6.1, 6.2)]*.

Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever). Immediately withhold ERLEADA® if ILD/pneumonitis is suspected. Permanently discontinue ERLEADA® in patients with severe ILD/pneumonitis or if no other potential causes of ILD/pneumonitis are identified *[see Dosage and Administration (2.2)]*.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

Embryo-Fetal Toxicity — The safety and efficacy of ERLEADA® have not been established in females. Based on findings from animals and 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

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%). In the SPARTAN study: anemia ERLEADA® 70% (0.4%), placebo 64% (0.5%); leukopenia ERLEADA® 47% (0.3%), placebo 29% (0%); lymphopenia ERLEADA® 41% (1.8%), placebo 21% (1.6%)
- **Chemistry —** In the TITAN study: hypertriglyceridemia ERLEADA® 17% (2.5%), placebo 12% (2.3%). In the SPARTAN study: hypercholesterolemia ERLEADA® 76% (0.1%), placebo 46% (0%); hyperglycemia ERLEADA® 70% (2%), placebo 59% (1.0%); hypertriglyceridemia ERLEADA® 67% (1.6%), placebo 49% (0.8%); hyperkalemia ERLEADA® 32% (1.9%), 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 and 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 1.5% 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 full Prescribing Information for ERLEADA®.

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Johnson&Johnson

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