Erleada® (apalutamide) 60 mg tablets 240 mg tablet

ERLEADA® is the first and only novel* androgen receptor inhibitor with 240 mg, single-tablet, once-daily dosing[1-3]

- Offers more flexibility with 240 mg tablet or 60 mg tablet†
- Provides alternate methods of administration for patients who have difficulty swallowing tablets whole or have a feeding tube
- Does not require concurrent chemotherapy[1]

Start early with ERLEADA®—with the option of one daily 240 mg tablet‡[1]

*ERLEADA® is a second generation androgen receptor inhibitor.
†The total dosage of ERLEADA® remains 240 mg per day.[1]
‡Patients receiving ERLEADA® should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

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.

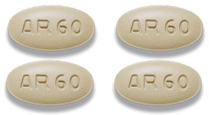
Please see full Important Safety Information throughout and on pages 6-7.

Please see enclosed full Prescribing Information for ERLEADA®.

ERLEADA® OFFERS MORE FLEXIBILITY FOR YOUR PATIENTS[1]

One 240 mg tablet or four 60 mg tablets — administered orally once daily.*[1]

60 mg tablet
4 tablets, once daily



(~17 mm x 9 mm)

240 mg tablet
1 tablet, once daily

(~21 mm x 10 mm)

Comparison of 60 mg and 240 mg tablets

Tablets shown are not actual size.[4]

No initial dose adjustments needed for renal or hepatic impairment†[1]

No need for concurrent chemotherapy

Do not crush or split tablets. ERLEADA® can be taken with or without food

Only ARI with alternate methods of dosing for patients who have difficulty swallowing tablets whole

*Patients receiving ERLEADA® should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

†ERLEADA® has not been evaluated in patients with severe renal or hepatic impairment.

ARI, androgen receptor inhibitor.

If Grade 3 or greater adverse reactions or other intolerable adverse reactions occur, withhold ERLEADA®. Consider permanent discontinuation of ERLEADA® for Grade 3 or 4 cerebrovascular and ischemic cardiovascular events. Permanently discontinue ERLEADA® for confirmed SCARs or for other Grade 4 skin reactions. For other adverse reactions, when symptoms improve to ≤Grade 1 or original grade, resume ERLEADA® at the same dose or a reduced dose (180 mg or 120 mg), if warranted.[1]

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (continued)

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.

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THE ONLY NOVEL‡ ANDROGEN RECEPTOR INHIBITOR IN JUST ONE DAILY 240 MG TABLET[1-3]

FDA-approved androgen receptor inhibitors§ for the treatment of mCSPC‖[1-3]

	Tablets Per Week	No Chemotherapy	Alternate Methods of Administration	Can Be Taken With or Without Food
ERLEADA® (apalutamide) 240 mg tablet/ 60 mg tablet	One 240 mg tablet QD OR Four 60 mg tablets QD	✓	✓¶	✓
Nubeqa® (darolutamide) 300 mg tablet	Two 300 mg tablets BID	Administered in combination with docetaxel	No alternate methods	With food
Xtandi® (enzalutamide) 40 mg tablet/ 80 mg tablet	Four 40 mg tablets QD OR Two 80 mg tablets QD	✓	No alternate methods	✓

‡ERLEADA® is a second generation ARI.

§Patients receiving these ARI therapies should also receive a GnRH analog concurrently or should have had bilateral orchiectomy.

‖Product comparisons with regard to efficacy and safety cannot be made in the absence of head-to-head clinical studies. This presentation is not intended to compare the relative efficacy or safety of the treatments. Please refer to the full Prescribing Information of each agent for dosage and administration.

¶For detailed instructions on administration, please see the full ERLEADA® Prescribing Information.

ARI, androgen receptor inhibitor; BID, twice a day; GnRH, gonadotropin-releasing hormone; mCSPC, metastatic castration-sensitive prostate cancer; QD, once daily.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (continued)

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.

Please see full Important Safety Information throughout and on pages 6-7.

Please see enclosed full Prescribing Information for ERLEADA®.

Erleada® (apalutamide) 60 mg tablets 240 mg tablet

THE ONLY ANDROGEN RECEPTOR INHIBITOR WITH THE CONVENIENCE OF ALTERNATE METHODS OF ADMINISTRATION[1-3]

ERLEADA® offers the convenience of alternate methods of administration for patients who have difficulty swallowing tablets whole or who have a feeding tube.*[1]

ERLEADA® 240 mg Tablets
Alternate Methods of Administration

Orange juice

Applesauce

Noncarbonated water

Feeding tube

ERLEADA® 60 mg Tablets
Alternate Method of Administration

Applesauce

*For detailed instructions on administration, please see the full ERLEADA® Prescribing Information.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (continued)

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.

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)*].

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FREQUENTLY ASKED QUESTIONS

What are the sizes of the 240 mg and 60 mg tablets?

The dimension of the 240 mg tablet is approximately 21 mm × 10 mm. The 60 mg tablet formulation is approximately 17 mm × 9 mm.[4]

Can the tablets be cut in half? Can the tablets be crushed or chewed?

No. Do not crush, chew, or split tablets. In patients who cannot swallow tablets whole, follow the instructions for the prescribed strength of ERLEADA® tablets for alternate methods of administration. The 240 mg tablet can be also prepared and given through a feeding tube. **For detailed instructions on administration, please see the full ERLEADA® Prescribing Information.**

Are the 240 mg and 60 mg tablets bioequivalent?

Yes. In a clinical bioequivalence study, the 240 mg apalutamide tablet was found to be bioequivalent to the 60 mg tablets. The 240 mg tablet met the bioequivalence criteria for all PK parameters of interest (C_{max} and $AUC_{0\text{-}72h}$). The 90% CI of the GMR of C_{max} and $AUC_{0\text{-}72h}$ were within the bioequivalence limits of 80-125%.[4]

Are there any differences in side effects/safety profiles between the 240 mg and 60 mg tablets?

In the clinical studies, following single-dose administration in healthy subjects, no new safety signals were identified.[4]

Can my patients still use the co-pay savings program?

Yes. The ERLEADA® Savings Program is available for both the 240 mg and 60 mg dose formulations.

AUC, area under the curve; CI, confidence interval; C_{max}, maximum serum concentration; GMR, geometric mean ratio; PK, pharmacokinetic.

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)*].

Erleada® (apalutamide) 60 mg tablets 240 mg tablet

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

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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)*].

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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, 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 accompanying full Prescribing Information for ERLEADA®.

cp-50507v6

Erleada® (apalutamide) 60 mg tablets 240 mg tablet

SCAN TO LEARN MORE ABOUT THE ONLY NOVEL ANDROGEN RECEPTOR INHIBITOR WITH THE OPTION OF ONE 240 MG DAILY TABLET[1-3]

Please see accompanying full Prescribing Information for ERLEADA®.

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. **4.** Data on file. Janssen Biotech, Inc.

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