ERLEADA® (apalutamide) tablets

--- ADVERSE REACTIONS ---

The most common adverse reactions (>10%) are fatigue, hypertension, rash, diarrhea, nausea, weight decreased, arthralgia, fall, hot flush, decreased appetite, fracture, and peripheral edema. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Products, LP at 1-800-526-7736 (1-800-JANSSEN or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

--- DRUG INTERACTIONS ---

- Concomitant use with medications that are sensitive substrates of CYP3A4, CYP2C19, CYP2C9, UGT, P-gp, BCRP, or OATP1B1 may result in loss of activity of these medications. (7.2)

- Females and Males of Reproductive Potential: Advise males with female partners of reproductive potential to use effective contraception. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 02/2018

--- FULL PRESCRIBING INFORMATION CONTENTS ---

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
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--- FULL PRESCRIBING INFORMATION ---

1 INDICATIONS AND USAGE

ERLEADA® is indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer (NM-CRPC).

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

ERLEADA 240 mg (four 60 mg tablets) administered orally once daily. Swallow tablets whole. ERLEADA can be taken with or without food. (2.1)

Patients should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy. (2.1)

2.2 Dose Modification

If a patient experiences a greater than or equal to Grade 3 toxicity or an intolerable side effect, hold dosing until symptoms improve to less than or equal to Grade 1 or original grade, then resume at the same dose or a reduced dose (180 mg or 120 mg), if warranted.

3 DOSAGE FORMS AND STRENGTHS

Tablets: 60 mg (3)

--- CONTRAINDICATIONS ---

- Females and Males of Reproductive Potential: Advise males with female partners of reproductive potential to use effective contraception. (8.3)

--- WARNINGS AND PRECAUTIONS ---

5.1 Falls and Fractures

Falls and fractures occurred in 16% and 12% of patients receiving ERLEADA, respectively. Evaluate patients for fracture and fall risk, and treat patients with bone targeted agents according to established guidelines. (5.1)

5.2 Seizure

Seizure occurred in 0.2% of patients receiving ERLEADA. Permanently discontinue ERLEADA in patients who develop a seizure during treatment. (5.2)

5.3 Females and Males of Reproductive Potential

Females and Males of Reproductive Potential: Advise males with female partners of reproductive potential to use effective contraception. (8.3)

--- ADVERSE REACTIONS ---

8.1 Further information is available in the full prescribing information and patient counseling information.

--- CLINICAL PHARMACOLOGY ---

12.1 Mechanism of Action

12.2 Pharmacodynamics

12.3 Pharmacokinetics

--- CLINICAL STUDIES ---

14.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

--- HOW SUPPLIED/STORAGE AND HANDLING ---

16.1 Clinical Trial Experience

--- PATIENT COUNSELING INFORMATION ---

17.1 Use in specific populations (8.3)

*Sections or subsections omitted from the full prescribing information are not listed.

--- ERROR ---

ERLEADATM (apalutamide) tablets, for oral use

These highlights do not include all the information needed to use ERLEADA safely and effectively. See full prescribing information for ERLEADA.
6 ADVERSE REACTIONS
The following are discussed in more detail in other sections of the labeling:

- Falls and Fractures [see Warnings and Precautions (5.1)].
- Seizure [see Warnings and Precautions (5.2)].

6.1 Clinical Trial Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

SPARTAN, a randomized (2:1), double-blind, placebo-controlled, multi-center clinical study, enrolled patients who had non-metastatic, castration-resistant prostate cancer (NM-CRPC). In this study, patients received either ERLEADA at a dose of 240 mg daily or a placebo. All patients in the SPARTAN study received a concomitant gonadotropin-releasing hormone (GnRH) analog or had a bilateral orchectomy. The median duration of exposure was 16.9 months (range: 0.1 to 42 months) in patients who received ERLEADA and 11.2 months (range: 0.1 to 37 months) in patients who received placebo.

Overall, 8 patients (1%) who were treated with ERLEADA died from adverse reactions. The reasons for death were infection (n=4), myocardial infarction (n=3), and cerebral hemorrhage (n=1). One patient (0.3%) treated with placebo died from an adverse reaction of cardiopulmonary arrest (n=1). ERLEADA was discontinued due to adverse reactions in 11% of patients, most commonly from rash (3%). Adverse reactions leading to dose interruption or reduction of ERLEADA occurred in 25% of patients; the most common (>1%) were rash, diarrhea, fatigue, nausea, vomiting, hypertension, and hematuria. Serious adverse reactions occurred in 25% of ERLEADA-treated patients and 23% in patients receiving placebo. The most common serious adverse reactions (>2%) were fracture (3%) in the ERLEADA arm and urinary retention (4%) in the placebo arm.

Table 1 shows adverse reactions occurring in >10% on the ERLEADA arm in SPARTAN that occurred with a 2% absolute increase in frequency compared to placebo. Table 2 shows laboratory abnormalities that occurred in ≥15% of patients, and urinary retention (4%) in the placebo arm.

Table 1: Adverse Reactions in SPARTAN

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>ERLEADA N=803</th>
<th>Placebo N=398</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Grades</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Grade 3-4</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Rash</td>
<td>24</td>
<td>6</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Injury, poisoning and procedural complications</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>Fall</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>Fracture</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Investigations</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Weight decreased</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>25</td>
<td>14</td>
</tr>
<tr>
<td>Hot flush</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>18</td>
<td>0</td>
</tr>
</tbody>
</table>

1 Includes fatigue and asthenia
2 Includes rash, rash maculo-papular, rash generalized, urticaria, rash pruritic, rash macular, conjunctivitis, erythema multiforme, rash papular, skin exfoliation, genital rash, rash erythematous, stomatitis, drug eruption, mouth ulceration, rash pustular, blister, papule, pemphigoid, skin erosion, and rash vesicular
4 Grade 4 definitions do not exist for these reactions

Table 2: Laboratory Abnormalities Occurring in ≥ 15% of ERLEADA-Treated Patients and at a Higher Incidence than Placebo (Between Arm Difference > 5% All Grades) in SPARTAN

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>ERLEADA N=803</th>
<th>Placebo N=398</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Grades</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Grade 3-4</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Hematology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>70</td>
<td>0.4</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>47</td>
<td>0.3</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>41</td>
<td>2</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>67</td>
<td>2</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>76</td>
<td>0.1</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>70</td>
<td>2</td>
</tr>
<tr>
<td>Hypocholesterolemia</td>
<td>29</td>
<td>0</td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>25</td>
<td>0.8</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>32</td>
<td>2</td>
</tr>
</tbody>
</table>

1 Does not reflect fasting values

Additional clinically significant adverse reactions occurring in 2% or more of patients treated with ERLEADA included hypothyroidism (8.1% versus 2% on placebo), pruritus (6.2% versus 2% on placebo), ischemic heart disease (3.7% versus 2% on placebo), and heart failure (2.2% versus 1% on placebo).

7 DRUG INTERACTIONS
7.1 Effect of Other Drugs on ERLEADA

Strong CYP2C9 or CYP3A4 Inhibitors
Co-administration of a strong CYP2C9 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties (sum of unbound apalutamide plus the potency-adjusted unbound N-desmethyl-apalutamide). No initial dose adjustment is necessary however, reduce the ERLEADA dose based on tolerability [see Dosage and Administration (2.2)]. Mild or moderate inhibitors of CYP2C9 or CYP3A4 are not expected to affect the exposure of apalutamide.

CYP3A4, CYP2C9, CYP2C19 and UGT Substrates
ERLEADA is a strong inducer of CYP3A4 and CYP2C19, and a weak inducer of CYP2C9. Co-administration 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 (UGT1) can result in decreased exposure. Use caution if substrates of UGT must be co-administered with ERLEADA and evaluate for loss of activity [see Clinical Pharmacology (12.3)].

P-gp, BCRP or OATP1B1 Substrates
Apalutamide was shown to be a weak inducer of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), and organic anion transporting polypeptide 1B1 (OATP1B1) clinically. At steady-state, apalutamide reduced the plasma exposure to fexofenadine (a P-gp substrate) and rosuvastatin (a BCRP/OATP1B1 substrate).
ERLEADATM (apalutamide) tablets

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 [see Clinical Pharmacology (12.3)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

ERLEADA is contraindicated for use in pregnant women because the drug can cause fetal harm and potential loss of pregnancy. ERLEADA is not indicated for use in females, so animal embryo-fetal developmental toxicity studies were not conducted with apalutamide. There are no human data on the use of ERLEADA in pregnant women. Based on its mechanism of action, ERLEADA may cause fetal harm when administered during pregnancy.

8.2 Lactation

Risk Summary

ERLEADA is not indicated for use in females. There are no data on the presence of apalutamide or its metabolites in human milk, the effect on the breastfed child, or the effect on milk production.

8.3 Females and Males of Reproductive Potential

Contraception

Males

Based on the mechanism of action and findings in an animal reproduction study, advise male patients 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)].

Infertility

Males

Based on animal studies, ERLEADA may impair fertility in males of reproductive potential [see Nonclinical Toxicology (13.1)].

8.4 Pediatric Use

Safety and effectiveness of ERLEADA in pediatric patients have not been established.

8.5 Geriatric Use

Of the 803 patients who received ERLEADA in SPARTAN, 87% of patients were 65 years and over and 49% were 75 years and over. Grade 3-4 adverse reactions occurred in 46% (323/697) of patients 65 years or older and in 51% (197/391) of patients 75 years or older treated with ERLEADA compared to 35% (124/355) of patients 65 years or older and 37% (70/187) of patients 75 years or older treated with placebo. No overall differences in effectiveness were observed between these patients and younger patients.

10 OVERDOSAGE

There is no known specific antidote for apalutamide overdose. In the event of an overdose, stop ERLEADA, undertake general supportive measures until clinical toxicity has been diminished or resolved.

11 DESCRIPTION

Apalutamide, the active ingredient of ERLEADA, is an androgen receptor inhibitor. The chemical name is (4-[7-(6-Cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide). Apalutamide is a white to slightly yellow powder. Apalutamide is practically insoluble in aqueous media over a wide range of pH values.

The molecular weight is 477.44 and molecular formula is C21H15F4N5O2S. The structural formula is:

![Structural formula of apalutamide](image)

ERLEADA (apalutamide) is supplied as film-coated tablets for oral administration containing 60 mg of apalutamide. Inactive ingredients of the core tablet are: colloidal anhydrous silica, croscarmellose sodium, hydroxypropyl methylcellulose-acetate succinate, magnesium stearate, microcrystalline cellulose, and silicified microcrystalline cellulose.

ERLEADATM (apalutamide) tablets

The tablets are finished with a commercially available film-coating comprising the following excipients: iron oxide black, iron oxide yellow, polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Apalutamide is an Androgen Receptor (AR) inhibitor that binds directly to the ligand-binding domain of the AR. Apalutamide inhibits AR nuclear translocation, inhibits DNA binding, and impedes AR-mediated transcription. A major metabolite, N-desmethyl apalutamide, is a less potent inhibitor of AR, and exhibited one-third the activity of apalutamide in an in vitro transcriptional reporter assay. Apalutamide administration caused decreased tumor cell proliferation and increased apoptosis leading to decreased tumor volume in mouse xenograft models of prostate cancer.

12.2 Pharmacodynamics

Cardiac Electrophysiology

The effect of apalutamide 240 mg once daily on the QTc interval was assessed in an open-label, uncontrolled, multi-center, single-arm dedicated QT study in 45 patients with CRPC. The maximum mean QTcF change from baseline was 12.4 ms (2-sided 90% upper CI: 16.0 ms). An exposure-QT analysis suggested a concentration-dependent increase in QTcF for apalutamide and its active metabolite.

12.3 Pharmacokinetics

Apalutamide pharmacokinetic parameters are presented as the mean [standard deviation (SD)] unless otherwise specified. Apalutamide Cmax and area under the concentration curve (AUC) increased proportionally following repeated once-daily dosing of 30 to 480 mg (0.125 to 2 times the recommended dosage). Following administration of the recommended dosage, apalutamide steady-state was achieved after 4 weeks and the mean accumulation ratio was approximately 5-fold. Apalutamide Cmax was 6.0 mcg/mL (1.7) and AUC was 100 mcg•h/mL (32) at steady-state. Daily fluctuations in apalutamide plasma concentrations were low, with mean peak-to-trough ratio of 1.63. An increase in apparent clearance (CL/F) was observed with repeat dosing, likely due to induction of apalutamide’s own metabolism. The auto-induction effect likely reached its maximum at the recommended dosage because exposure of apalutamide across the dose range of 30 to 480 mg is dose-proportional.

The major active metabolite N-desmethyl apalutamide Cmax was 5.9 mcg/mL (1.0) and AUC was 124 mcg•h/mL (23) at steady-state after the recommended dosage. N-desmethyl apalutamide was characterized by a flat concentration-time profile at steady-state with a mean peak-to-trough ratio of 1.27. Mean AUC metabolite/parent drug ratio for N-desmethyl apalutamide following repeat-dose administration was 1.3. Based on systemic exposure, relative potency, and pharmacokinetic properties, N-desmethyl apalutamide likely contributed to the clinical activity of apalutamide.

Absorption

Mean absolute oral bioavailability was approximately 100%. Median time to achieve peak plasma concentration (tmax) was 2 hours (range: 1 to 5 hours).

Effect of Food

Administration of apalutamide to healthy subjects under fasting conditions and with a high-fat meal (approximately 500 to 600 fat calories, 250 carbohydrate calories, and 150 protein calories) resulted in no clinically relevant changes in Cmax and AUC. Median time to reach tmax was delayed approximately 2 hours with food.

Distribution

The mean apparent volume of distribution at steady-state of apalutamide was approximately 276 L.

Apalutamide was 96% and N-desmethyl apalutamide was 95% bound to plasma proteins with no concentration dependency.

Elimination

The CL/F of apalutamide was 1.3 L/h after single dosing and increased to 2.0 L/h at steady-state after once-daily dosing likely due to CYP3A4 auto-induction. The mean effective half-life of apalutamide in patients was approximately 3 days at steady-state.

Metabolism

Metabolism is the main route of elimination of apalutamide. Apalutamide is primarily metabolized by CYP2C8 and CYP3A4 to form active metabolite, N-desmethyl apalutamide. The contribution of CYP2C8 and CYP3A4 in the metabolism of apalutamide is estimated to be 58% and 13% following single dose changes to 40% and 37%, respectively at steady-state.

Apalutamide represented 45% and N-desmethyl apalutamide represented 44% of the total AUC following a single oral administration of radiolabeled apalutamide 240 mg.
Effect of Other Drugs on ERLEADA

**Strong CYP2C8 inhibitors**
Apalutamide $C_{\text{max}}$ decreased by 21% while AUC increased by 68% following co-administration of ERLEADA as a 240 mg single dose with gemfibrozil (a strong CYP2C8 inhibitor). Gemfibrozil is predicted to increase the steady-state apalutamide $C_{\text{max}}$ by 32% and AUC by 44%. For the active moieties (sum of unbound apalutamide plus the potency-adjusted unbound N-desmethyl apalutamide), the predicted steady-state $C_{\text{max}}$ increased by 19% and AUC by 23%.

**Strong CYP3A4 inhibitors**
Apalutamide $C_{\text{max}}$ decreased by 22% while AUC was similar following co-administration of ERLEADA as a 240 mg single dose with itraconazole (a strong CYP3A4 inhibitor). Ketocanazole (a strong CYP3A4 inhibitor) is predicted to increase the single-dose apalutamide AUC by 24% but have no impact on $C_{\text{max}}$. Ketocanazole is predicted to increase the steady-state apalutamide $C_{\text{max}}$ by 38% and AUC by 51%. For the active moieties, the predicted steady-state $C_{\text{max}}$ increased by 23% and AUC by 28%.

**CYP3A4/CYP2C8 inducers**
Rifampin (a strong CYP3A4 and moderate CYP2C8 inducer) is predicted to decrease the steady-state apalutamide $C_{\text{max}}$ by 25% and AUC by 34%. For the active moieties, the predicted steady-state $C_{\text{max}}$ decreased by 15% and AUC by 19%.

**Acid lowering agents**
Apalutamide is not ionizable under relevant physiological pH condition, therefore acid lowering agents (e.g., proton pump inhibitor, H$_2$-receptor antagonist, antacid) are not expected to affect the solubility and bioavailability of apalutamide.

**Drugs affecting transporters**
In vitro, apalutamide and N-desmethyl apalutamide are substrates for P-gp but not BCRP, OATP1B1, and OATP1B3. Because apalutamide is completely absorbed after oral administration, P-gp does not limit the absorption of apalutamide and therefore, inhibition or induction of P-gp is not expected to affect the bioavailability of apalutamide.

**Effect of ERLEADA on Other Drugs**

**CYP substrates**
In vitro studies showed that apalutamide and N-desmethyl apalutamide are moderate to strong CYP3A4 and CYP2B6 inducers, are moderate inhibitors of CYP2B6 and CYP2C8, and weak inhibitors of CYP2C9, CYP2C19, and CYP3A4. Apalutamide and N-desmethyl apalutamide do not affect CYP1A2 and CYP2D6 at therapeutically relevant concentrations.

**P-gp, BCRP and OATP1B1 substrates**
Co-administration of ERLEADA with single oral doses of sensitive CYP substrates resulted in a 92% decrease in the AUC of midazolam (a CYP3A4 substrate), 85% decrease in the AUC of omeprazole (a CYP2C19 substrate), and 46% decrease in the AUC of S-warfarin (a CYP2C9 substrate). ERLEADA did not cause clinically significant changes in exposure to a CYP2C8 substrate.

**UGT substrates**
Apalutamide may induce UGT. Concomitant administration of ERLEADA with medications that are substrates of UGT may result in lower exposure to these medications.
Figure 1: Kaplan-Meier Metastasis-Free Survival (MFS) Curve in SPARTAN

Table 3: BICR-assessed Efficacy Results (SPARTAN)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Number of Events (%)</th>
<th>Median [Months (95% CI)]</th>
<th>HR (95% CI)</th>
<th>p-value (log-rank test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastasis Free Survival</td>
<td>ERLEADA (N=806)</td>
<td>184 (23%)</td>
<td>40.51 (NE, NE)</td>
<td>16.20 (14.59, 18.40)</td>
</tr>
<tr>
<td></td>
<td>Placebo (N=401)</td>
<td>194 (48%)</td>
<td>13.5</td>
<td>0.27 (0.22, 0.34) &lt;0.0001</td>
</tr>
<tr>
<td>Time to Metastasis</td>
<td>ERLEADA (N=806)</td>
<td>175 (22%)</td>
<td>40.51 (NE, NE)</td>
<td>16.59 (14.59, 18.46)</td>
</tr>
<tr>
<td></td>
<td>Placebo (N=401)</td>
<td>191 (48%)</td>
<td>14.72</td>
<td></td>
</tr>
<tr>
<td>Progression-Free Survival</td>
<td>ERLEADA (N=806)</td>
<td>200 (25%)</td>
<td>40.51 (NE, NE)</td>
<td>14.72 (14.49, 18.37)</td>
</tr>
<tr>
<td></td>
<td>Placebo (N=401)</td>
<td>204 (51%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 All analyses stratified by PSA doubling time, bone-sparing agent use, and locoregional disease status.
NE=Not Estimable

16 HOW SUPPLIED/STORAGE AND HANDLING
ERLEADA (apalutamide) 60 mg film-coated tablets are slightly yellowish to greyish green, oblong-shaped tablets debossed with “AR 60” on one side. ERLEADA 60 mg tablets are available in bottles of 120 tablets. Each bottle contains silica gel desiccant.

NDC Number 59676-600-12

Storage and Handling
Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Store in the original package. Do not discard desiccant. Protect from light and moisture.

ERLEADA (apalutamide) tablets

17 PATIENT COUNSELING INFORMATION
Advising the patient to read the FDA-approved patient labeling (Patient Information).

Falls and Fractures
- Inform patients that ERLEADA is associated with an increased incidence of falls and fractures [see Warnings and Precautions (5.1)].

Seizures
- Inform patients that ERLEADA 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 experience a seizure [see Warnings and Precautions (5.2)].

Rash
- Inform patients that ERLEADA is associated with rashes and to inform their healthcare provider if they develop a rash [see Adverse Reactions (6.1)].

Dosage and Administration
- Inform patients receiving concomitant gonadotropin-releasing hormone (GnRH) analog therapy that they need to maintain this treatment during the course of treatment with ERLEADA.
- Instruct patients to take their dose at the same time each day (once daily). ERLEADA can be taken with or without food. Each tablet should be swallowed whole.
- Inform patients that in the event of a missed daily dose of ERLEADA, they should take their normal dose as soon as possible on the same day with a return to the normal schedule on the following day. The patient should not take extra tablets to make up the missed dose [see Dosage and Administration (2.1)].

Embryo-Fetal Toxicity
- Inform patients that ERLEADA can be harmful to a developing fetus. Advise patients having sex with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA. Advise male patients to use a condom if having sex with a pregnant woman [see Use in Specific Populations (8.1, 8.3)].

Infertility
- Advise male patients that ERLEADA may impair fertility and not to donate sperm during therapy and for 3 months following the last dose of ERLEADA [see Use in Specific Populations (8.3)].

Manufactured by:
Janssen Ortho LLC
Gurabo, PR 00778

Manufactured for:
Janssen Products, LP
Horsham, PA 19044

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PATIENT INFORMATION
ERLEADA™ (er lee’dah)
(apalutamide)
Tablets

What is ERLEADA?
ERLEADA is a prescription medicine used to treat prostate cancer that has not spread to other parts of the body and no longer responds to a medical or surgical treatment that lowers testosterone.
It is not known if ERLEADA is safe or effective in children.

Do not take ERLEADA if you:
• are pregnant or may become pregnant. ERLEADA may harm your unborn baby.
• are female. ERLEADA is not for use in women.

Before taking ERLEADA, tell your healthcare provider about all your medical conditions, including if you:
• have a history of seizures, brain injury, stroke, or brain tumors
• have a partner who is pregnant or may become pregnant. Men who are sexually active with a pregnant woman must use a condom during and for 3 months after treatment with ERLEADA. If your sexual partner may become pregnant, an effective birth control (contraception) must be used during and for 3 months after treatment. Talk with your healthcare provider if you have questions about birth control.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. ERLEADA can interact with many other medicines.

You should not start or stop any medicine before you talk with the healthcare provider that prescribed ERLEADA.

Know the medicines you take. Keep a list of them with you to show to your healthcare provider and pharmacist when you get a new medicine.

How should I take ERLEADA?
• Take ERLEADA exactly as your healthcare provider tells you.
• Take your prescribed dose of ERLEADA 1 time a day, at the same time each day.
• Take ERLEADA with or without food.
• Swallow ERLEADA tablets whole.
• Your healthcare provider may change your dose if needed.
• Do not stop taking your prescribed dose of ERLEADA without talking with your healthcare provider first.
• If you miss a dose of ERLEADA, take your normal dose as soon as possible on the same day. Return to your normal schedule on the following day. You should not take extra tablets to make up the missed dose.
• If you take too much ERLEADA, call your healthcare provider or go to the nearest hospital emergency room.
• Your healthcare provider may do blood tests to check for side effects.

What are the possible side effects of ERLEADA?
ERLEADA may cause serious side effects including:
• Falls and fractures. ERLEADA treatment can cause bones and muscles to weaken and may increase your risk for falls and fractures. Falls and fractures have happened in people during treatment with ERLEADA. Falls were not caused by loss of consciousness (fainting) or seizures. Your healthcare provider will monitor your risks for falls and fractures during treatment with ERLEADA.
• Seizure. If you take ERLEADA, you may be at risk of having a seizure. You should avoid activities where a sudden loss of consciousness could cause serious harm to yourself or others. Tell your healthcare provider right away if you have a loss of consciousness or seizure. Your healthcare provider will stop ERLEADA if you have a seizure during treatment.

The most common side effects of ERLEADA include:
• feeling very tired
• high blood pressure
• rash
• diarrhea
• nausea
• decreased appetite
• weight loss
• joint pain
• fall
• hot flash
• bone injury (fracture)
• swollen hands, ankles, or feet

ERLEADA may cause fertility problems in males, which may affect the ability to father children. Talk to your healthcare provider if you have concerns about fertility. Do not donate sperm during treatment with ERLEADA and for 3 months after the last dose of ERLEADA.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of ERLEADA.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.
**How should I store ERLEADA?**

- Store ERLEADA at room temperature between 68°F to 77°F (20°C to 25°C).
- Store ERLEADA in the original package.
- The bottle of ERLEADA contains a desiccant packet to help keep your medicine dry (protect it from moisture). Do not throw away (discard) the desiccant.
- Protect ERLEADA from light and moisture.

*Keep ERLEADA and all medicines out of the reach of children.*

**General information about the safe and effective use of ERLEADA.**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use ERLEADA for a condition for which it was not prescribed. Do not give ERLEADA to other people, even if they have the same symptoms that you have. It may harm them.

If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about ERLEADA that is written for health professionals.

**What are the ingredients in ERLEADA?**

**Active ingredient:**

apalutamide

**Inactive ingredients:**

colloidal anhydrous silica, croscarmellose sodium, hydroxypropyl methylcellulose-acetate succinate, magnesium stearate, microcrystalline cellulose, and silicified microcrystalline cellulose. The film-coating contains iron oxide black, iron oxide yellow, polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide.

*Manufactured by:* Janssen Ortho LLC, Gurabo, PR 00778  
*Manufactured for:* Janssen Products, LP, Horsham, PA 19044  
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For more information, call Janssen Products, LP at 1-800-526-7736 (1-800-JANSSEN) or go to www.erleada.com.