Apalutamide

■ Apalutamide, a nonsteroidal antiandrogen, is an antineoplastic agent.

Uses

■ **Prostate Cancer** Apalutamide is used for the treatment of nonmetastatic castration-resistant prostate cancer.

The current indication for apalutamide is based principally on the results of a randomized, double-blind, placebo-controlled phase 3 study (SPARTAN) in 1207 patients with nonmetastatic castration-resistant prostate cancer who were at high risk for metastasis (i.e., prostate specific antigen [PSA] doubling time of 10 months or less despite continuous androgen deprivation therapy). Patients were randomized in a 2:1 ratio to receive either apalutamide (240 mg once daily) or placebo; androgen deprivation therapy was continued in all patients. Patients were stratified by PSA doubling time, use of bone resorption inhibitors, and presence of locoregional nodal disease. Treatment was continued until disease progression or unacceptable toxicity occurred, new treatment was initiated, or the patient withdrew from the study. The primary measure of efficacy was metastasis-free survival; secondary end points included time to metastasis, progression-free (including locoregional or distant metastatic progression) survival, time to symptomatic progression, and overall survival. The median age of patients enrolled in the study was 74 years; 26% of patients were 80 years of age or older. Most patients (77%) had undergone prior surgery or radiation therapy of the prostate; 78% had a Gleason score of 7 or higher, 73% had received prior treatment with a nonsteroidal antiandrogen (69% had received bicalutamide and 10% had received flutamide), and all had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.

At a median follow-up of 20.3 months, metastasis-free survival was substantially longer in apalutamide-treated patients compared with those who received placebo (40.5 and 16.2 months, respectively). Results of a subgroup analysis (based on PSA doubling time, baseline PSA concentration, number of prior hormonal therapies, use of bone resorption inhibitors, locoregional nodal disease, age, race, ECOG performance status, and geographic region) suggested that the drug's effect on metastasis-free survival was consistent across all subgroups. Patients receiving apalutamide also had longer time to metastasis, progression-free survival, and time to symptomatic progression compared with those receiving placebo. Overall survival had not been reached at the time of primary analysis; the study was terminated early because clinical benefit of apalutamide had been demonstrated.

Dosage and Administration

■ **General** Patients receiving apalutamide should receive concurrent therapy with a gonadotropin-releasing hormone (GnRH) analog unless they have undergone bilateral orchiectomy.

Restricted Distribution Apalutamide is available only through specialty pharmacies. Clinicians may contact Janssen CarePath at 877-227-3728 or consult the Janssen CarePath website for specific availability information (https://www.janssencarepath.com/hcp/erleada).

■ **Administration** Apalutamide is administered orally once daily without regard to food. The tablets should be swallowed whole.

■ **Dosage** ***Prostate Cancer*** For the treatment of nonmetastatic castration-resistant prostate cancer, the recommended dosage of apalutamide is 240 mg once daily. In the principal efficacy study, therapy was continued until disease progression or unacceptable toxicity occurred.

Dosage Modification for Toxicity **General Toxicity.** If an intolerable adverse effect or grade 3 or greater toxicity occurs, apalutamide therapy should be interrupted until symptoms improve to grade 1 or less or return to baseline. Apalutamide therapy may then be resumed with or without a dosage reduction. If a dosage reduction is warranted, the dosage of apalutamide may be reduced to 180 or 120 mg daily.

■ **Special Populations** Initial dosage adjustment is not necessary in patients with mild or moderate hepatic impairment (Child-Pugh class A or B). (See Hepatic Impairment under Warnings/Precautions: Specific Populations, in Cautions.)

Initial dosage adjustment is not necessary in patients with mild or moderate renal impairment (estimated glomerular filtration rate [eGFR] of 30–89 mL/minute per 1.73 m^2). (See Renal Impairment under Warnings/Precautions: Specific Populations, in Cautions.)

The manufacturer makes no special dosage recommendations for geriatric patients; most patients (87%) in the principal efficacy study were 65 years of age or older. (See Geriatric Use under Warnings/Precautions: Specific Populations, in Cautions.)

Cautions

■ **Contraindications** Apalutamide is contraindicated in pregnant women. (See Pregnancy under Warnings/Precautions: Specific Populations, in Cautions.)

■ **Warnings/Precautions** ***Falls and Fractures*** Falls and fractures have occurred in patients receiving apalutamide. In the principal efficacy study in patients with nonmetastatic castration-resistant prostate cancer, falls were reported in 16% of patients receiving apalutamide compared with 9% of those receiving placebo and were not associated with loss of consciousness or seizure. Fractures were reported in 12% of apalutamide-treated patients compared with 7% of those receiving placebo; grade 3 or 4 fractures occurred in 3% of patients receiving the drug compared with 1% of those receiving placebo. The median time to onset of fracture was 314 days (range: 20–953 days) in patients receiving apalutamide. Routine bone density assessments were not performed during the study. In addition, patients receiving bone resorption inhibitors (e.g., denosumab, zoledronic acid) at dosages recommended for prevention of tumor-related skeletal events were excluded from the study, and relatively few patients received these agents at dosages recommended for prevention of bone loss in the setting of osteoporosis.

Patients receiving apalutamide should be evaluated for fracture and fall risk. Patients at risk for fractures should be monitored and managed according to established treatment guidelines; therapy with bone resorption inhibitors should be considered.

Seizures Seizures have occurred in patients receiving apalutamide. In the principal efficacy study in patients with nonmetastatic castration-resistant prostate cancer, seizure was reported in 0.2% of patients receiving apalutamide compared with none of those receiving placebo. Patients with predisposing factors for seizures (e.g., history of seizure, concomitant use of drugs that lower the seizure threshold or induce seizures) were excluded from the study. Time to onset of seizures ranged from 354–475 days following initiation of the drug.

It is not known whether anticonvulsants will prevent seizures in patients receiving apalutamide. The safety of resuming apalutamide therapy in patients who experienced a seizure while receiving the drug has not been established. Apalutamide should be permanently discontinued in patients who develop a seizure during treatment. (See Advice to Patients.)

Fetal/Neonatal Morbidity and Mortality Based on its mechanism of action, apalutamide may cause fetal harm. The drug is contraindicated in pregnant women. Based on findings in an animal reproduction and fertility study, men with female partners of childbearing potential should use effective methods of contraception during apalutamide therapy and for 3 months after the last dose of the drug; in addition, men should not donate sperm while receiving the drug and for 3 months after the drug is discontinued. Patients receiving the drug should use a condom during sexual encounters with pregnant women.

Impairment of Male Fertility Based on animal studies, apalutamide may impair male fertility. In male rats, apalutamide was associated with decreased sperm concentration and motility, increased abnormal sperm morphology, reduced epididymis and secondary sex gland weights, lower copulation and fertility rates upon pairing with untreated females, and a reduced number of live fetuses secondary to increased pre- and/or post-implantation loss; effects on male rats were reversible following discontinuance of drug administration.

Specific Populations **Pregnancy.** Based on its mechanism of action, apalutamide can cause fetal harm and potential loss of pregnancy if administered to pregnant women. The drug is contraindicated in pregnant women. (See Fetal/Neonatal Morbidity and Mortality under Cautions: Warnings/Precautions.)

Lactation. It is not known whether apalutamide or its metabolites are distributed into milk; the drug is not indicated for use in women. The effects of apalutamide on nursing infants or on milk production are not known.

Pediatric Use. Safety and efficacy of apalutamide have not been established in pediatric patients.

Geriatric Use. In the principal efficacy study evaluating apalutamide in men with nonmetastatic castration-resistant prostate cancer, 87% of patients were 65 years of age or older and 49% were 75 years of age or older. No overall differences in efficacy were observed between geriatric patients and younger adults. Among patients 65 years of age or older, grade 3 or 4 adverse reactions were reported in 46% of apalutamide-treated patients compared with 35% of placebo recipients; among patients 75 years of age or older, the respective frequencies were 51 and 37%.

Hepatic Impairment. No clinically important differences in systemic exposure of apalutamide or *N*-desmethylapalutamide were observed in patients with mild or moderate hepatic impairment (Child-Pugh class A or B) compared with individuals with normal hepatic function. The unbound fraction of apalutamide or *N*-desmethylapalutamide was not affected by hepatic impairment.

Pharmacokinetics of apalutamide have not been established in patients with severe hepatic impairment (Child-Pugh class C).

Renal Impairment. Renal impairment is not expected to affect the elimination of apalutamide or *N*-desmethylapalutamide. No clinically important differences in systemic exposure of apalutamide or *N*-desmethylapalutamide were observed in patients with mild or moderate renal impairment (estimated glomerular filtration rate [eGFR] of 30–89 mL/minute per 1.73 m^2) compared with individuals with normal renal function.

Pharmacokinetics of apalutamide have not been established in patients with severe renal impairment (eGFR of 29 mL/minute or less per 1.73 m^2).

■ **Common Adverse Effects** Adverse effects reported in 10% or more of patients receiving apalutamide and at an incidence at least 2% higher than that reported with placebo include fatigue/asthenia, hypertension, rash, diarrhea, nausea, weight loss, arthralgia, falls, hot flush, decreased appetite, fracture, and peripheral edema.

Laboratory abnormalities reported in 15% or more of patients receiving apalutamide and at an incidence more than 5% higher than that reported with placebo include hypercholesterolemia, hyperglycemia, anemia, hypertriglyceridemia, leukopenia, lymphopenia, and hyperkalemia.

Drug Interactions

Apalutamide is metabolized principally by cytochrome P-450 (CYP) isoenzymes 2C8 and 3A4 to form its major active metabolite, *N*-desmethylapalutamide.

Apalutamide is a potent inducer of CYP3A4 and 2C19 and a weak inducer of CYP2C9 in humans. In addition, in vitro studies indicate that apalutamide and *N*-desmethylapalutamide are moderate to potent inducers of CYP3A4 and 2B6, moderate inhibitors of CYP2B6 and 2C8, and weak inhibitors of CYP2C9, 2C19, and 3A4. Apalutamide and *N*-desmethylapalutamide neither inhibit nor induce CYP1A2 or 2D6 at clinically relevant concentrations.

Apalutamide and *N*-desmethylapalutamide are substrates of P-glycoprotein (P-gp) in vitro; however, apalutamide absorption is not limited by P-gp. Apalutamide and *N*-desmethylapalutamide are not substrates of breast cancer resistance protein (BCRP), organic anion transport protein (OATP) 1B1, or OATP1B3.

Apalutamide is a weak inducer of P-gp, BCRP, and OATP1B1 in humans. In vitro, apalutamide and *N*-desmethylapalutamide inhibit organic cation transporter 2 (OCT2), organic anion transporter 3 (OAT3), and multidrug and toxin extrusion (MATE) transporters. Apalutamide may induce uridine diphosphate-glucuronosyltransferase (UGT). Apalutamide and *N*-desmethylapalutamide do not inhibit organic anion transporter 1 (OAT1).

■ **Drugs Affecting Hepatic Microsomal Enzymes** Concomitant use of apalutamide with potent inhibitors of CYP2C8 or 3A4 may result in increased steady-state exposure of the total active forms of apalutamide (i.e., unbound apalutamide plus potency-adjusted unbound *N*-desmethylapalutamide). No initial dosage adjustment is necessary; however, reduction of apalutamide dosage may be necessary based on tolerability. (See General Toxicity under Dosage: Dosage Modification for Toxicity, in Dosage and Administration.)

Mild or moderate inhibitors of CYP2C8 or 3A4 are not expected to affect the exposure of apalutamide.

Concomitant use of apalutamide with inducers of CYP2C8 and/or 3A4 may decrease steady-state apalutamide concentrations.

■ **Drugs Metabolized by Hepatic Microsomal Enzymes** Concomitant use of apalutamide with drugs that are principally metabolized by CYP3A4, 2C9, or 2C19 may result in decreased exposure of the CYP substrate. The manufacturer of apalutamide recommends that concomitant use be avoided when possible (e.g., by switching to an alternative drug that is not metabolized by these isoenzymes); if concomitant use cannot be avoided, patients should be monitored for decreased therapeutic effect of the CYP substrate.

Concomitant administration of apalutamide with a CYP2C8 substrate did not result in clinically important changes in exposure of the CYP2C8 substrate. (See Drug Interactions: Pioglitazone.)

■ **Drugs Affecting or Affected by P-glycoprotein Transport** Inhibition or induction of P-gp is not expected to affect the bioavailability of apalutamide.

Concomitant use of apalutamide and P-gp substrates may result in decreased exposure of the P-gp substrate. If concomitant use is necessary, caution should be exercised and patients should be monitored for decreased therapeutic effect of the P-gp substrate.

■ **Drugs Affected by Breast Cancer Resistance Protein and/or Organic Anion Transport Polypeptide 1B1** Concomitant use of apalutamide with drugs that are substrates of BCRP or OATP1B1 may result in decreased exposure of the BCRP or OATP1B1 substrate. If concomitant use is necessary, caution should be exercised and patients should be monitored for decreased therapeutic effect of the BCRP or OATP1B1 substrate.

■ **Drugs Metabolized by Uridine Diphosphate-glucuronosyltransferase** Concomitant use of apalutamide with drugs that are substrates of UGT may result in decreased exposure of the UGT substrate. If concomitant use is necessary, caution should be exercised and patients should be monitored for decreased therapeutic effect of the UGT substrate.

■ **Drugs Affected by Other Transporters** In vitro, apalutamide and *N*-desmethylapalutamide inhibit OCT2, OAT3, and MATE transporters, but do not inhibit OAT1. Apalutamide is not expected to cause clinically important changes in exposure of OAT3 substrates (e.g., penicillin G).

■ **Drugs Affecting Gastric Acidity** Because apalutamide remains unionized at physiologic pH, concomitant administration of apalutamide and drugs that increase gastric pH (e.g., proton-pump inhibitors, histamine H_2-receptor antagonists, antacids) are not expected to have a clinically important effect on the solubility and bioavailability of apalutamide.

■ **Antifungal Agents** ***Itraconazole*** Concomitant administration of the potent CYP3A4 inhibitor itraconazole (200 mg daily for 32 days) and apalutamide (single 240-mg dose) decreased peak plasma concentrations of apalutamide and *N*-desmethylapalutamide by 22 and 15%, respectively; areas under the concentration-time curve (AUCs) were not affected.

No initial dosage adjustment is necessary; however, reduction of apalutamide dosage may be necessary based on tolerability in patients receiving concomitant itraconazole therapy. (See General Toxicity under Dosage: Dosage Modification for Toxicity, in Dosage and Administration.)

Ketoconazole Based on pharmacokinetic modeling, concomitant use of ketoconazole (a potent CYP3A4 inhibitor) and apalutamide is expected to increase AUC of single-dose apalutamide by 24% with no change in apalutamide peak plasma concentration, and to increase steady-state AUC and peak plasma concentration of apalutamide by 51 and 38%, respectively. At steady state, AUC and peak plasma concentration of the total active forms of apalutamide (i.e., unbound apalutamide plus potency-adjusted unbound *N*-desmethylapalutamide) are expected to increase by 28 and 23%, respectively.

No initial dosage adjustment is necessary; however, reduction of apalutamide dosage may be necessary based on tolerability in patients receiving concomitant ketoconazole therapy. (See General Toxicity under Dosage: Dosage Modification for Toxicity, in Dosage and Administration.)

■ **Abiraterone** In an open-label phase 1b trial in patients with progressive metastatic castration-resistant prostate cancer treated with abiraterone acetate (1 g daily) and prednisone (5 mg twice daily), addition of apalutamide (240 mg daily) did not result in clinically important changes in the pharmacokinetics of apalutamide or abiraterone.

■ **Fexofenadine** Concomitant administration of the P-gp substrate fexofenadine (single dose) and apalutamide (240 mg daily at steady state) decreased fexofenadine AUC by 30%. If concomitant use of fexofenadine and apalutamide is necessary, caution should be exercised and patients should be monitored for decreased therapeutic effect of fexofenadine.

■ **Gemfibrozil** Concomitant administration of the potent CYP2C8 inhibitor gemfibrozil (600 mg twice daily for 32 days) and apalutamide (single 240-mg dose) decreased peak plasma concentration of apalutamide by 21% and increased AUC of apalutamide by 68%. Based on pharmacokinetic modeling, gemfibrozil is expected to increase steady-state AUC and peak plasma concentrations of apalutamide by 44 and 32%, respectively, and to increase steady-state AUC and peak plasma concentrations of the total active forms of apalutamide (i.e., unbound apalutamide plus potency-adjusted unbound *N*-desmethylapalutamide) by 23 and 19%, respectively.

No initial dosage adjustment is necessary; however, reduction of apalutamide dosage may be necessary based on tolerability in patients receiving concomitant gemfibrozil therapy. (See General Toxicity under Dosage: Dosage Modification for Toxicity, in Dosage and Administration.)

■ **Midazolam** Concomitant administration of the CYP3A4 substrate midazolam (single oral dose) and apalutamide (240 mg daily) decreased midazolam AUC by 92%. Concomitant use of apalutamide and midazolam should be avoided when possible (e.g., by switching to an alternative drug that is not metabolized by CYP3A4); if concomitant use cannot be avoided, patients should be monitored for decreased therapeutic effect of midazolam.

■ **Omeprazole** Concomitant administration of the CYP2C19 substrate omeprazole (single dose) and apalutamide (240 mg daily) decreased omeprazole AUC by 85%. Concomitant use of apalutamide and omeprazole should be avoided when possible (e.g., by switching to an alternative drug that is not metabolized by CYP2C19); if concomitant use cannot be avoided, patients should be monitored for decreased therapeutic effect of omeprazole.

■ **Pioglitazone** Concomitant administration of the CYP2C8 substrate pioglitazone (single dose) and apalutamide (240 mg daily) decreased pioglitazone AUC by 18%.

■ **Prednisone** In an open-label phase 1b trial in patients with progressive metastatic castration-resistant prostate cancer treated with abiraterone acetate (1 g daily) and prednisone (5 mg twice daily), addition of apalutamide (240 mg daily) did not result in clinically important changes in the pharmacokinetics of apalutamide or abiraterone.

■ **Rifampin** Based on pharmacokinetic modeling, concomitant use of the potent CYP3A4 and moderate CYP2C8 inducer rifampin (600 mg daily) and apalutamide is expected to decrease steady-state AUC and peak plasma concentrations of apalutamide by 34 and 25%, respectively, and to decrease steady-state AUC and peak plasma concentrations of the total active forms of apalutamide (i.e., unbound apalutamide plus potency-adjusted unbound *N*-desmethylapalutamide) by 19 and 15%, respectively. However, no pharmacokinetic interactions were observed between apalutamide and CYP3A4 inducers in a population pharmacokinetic analysis based on limited data.

■ **Rosuvastatin** Concomitant administration of the BCRP and OATP1B1 substrate rosuvastatin (single dose) and apalutamide (240 mg daily) decreased rosuvastatin AUC by 41% with no change in rosuvastatin peak plasma concentration. If concomitant use of rosuvastatin and apalutamide is necessary, caution should be exercised and patients should be monitored for decreased therapeutic effect of rosuvastatin.

■ **Warfarin** Concomitant administration of the CYP2C9 substrate warfarin (single dose) and apalutamide (240 mg daily) decreased AUC of *S*-warfarin by 46%. If apalutamide is used concomitantly with warfarin, international normalized ratio (INR) should be monitored at initiation of concomitant therapy and upon discontinuance of apalutamide.

Description

Apalutamide, a nonsteroidal antiandrogen, is an antineoplastic agent. The drug competitively inhibits androgen binding to androgen receptors; its mechanisms of action are similar to those of enzalutamide. Apalutamide binds directly to the ligand-binding domain of the androgen receptor and inhibits nuclear translocation of the activated androgen receptor, androgen-dependent binding of the androgen receptor complex to DNA, and androgen receptor-mediated gene transcription in cells that overexpress the androgen receptor. Apalutamide reduced tumor growth and induced apoptosis of tumor cells, leading to decreased tumor volume, in xenograft models of castration-resistant prostate cancer in mice.

In castration-resistant prostate cancer, alterations in androgen receptor signaling (e.g., androgen receptor gene mutation or amplification, androgen receptor overexpression) have been shown to result in persistence of androgen receptor signaling and to contribute to disease progression despite castrate levels of androgens. Resistance to conventional antiandrogens (e.g., bicalutamide, flutamide, nilutamide) in castration-resistant prostate cancer has been associated with paradoxical agonistic effects of these drugs and continued androgen receptor signaling. Unlike these conventional antiandrogens but similar to enzalutamide, apalutamide does not exhibit agonistic activity in cells that overexpress the androgen receptor.

The binding affinity of apalutamide at the androgen receptor is 7–10 times greater than that of bicalutamide. Although apalutamide and enzalutamide exhibit similar antiandrogenic activity in vitro, apalutamide demonstrated greater activity than enzalutamide in xenograft models of castration-resistant prostate cancer. At equivalent dosages, steady-state concentrations of apalutamide and enzalutamide in xenograft tumors in mice were similar, but steady-state plasma and CNS concentrations of apalutamide were twofold to fourfold lower and fourfold lower, respectively, compared with concentrations of enzalutamide. Whether these higher murine tumor-to-plasma and tumor-to-CNS ratios for apalutamide translate into a lower risk of adverse effects, including seizures and other CNS toxicity, remains to be established.

Apalutamide exhibits dose-proportional pharmacokinetics over a dosage range of 30–480 mg once daily. Following oral administration, the median time to peak plasma concentrations is 2 hours; the mean absolute bioavailability of apalutamide is approximately 100%. Steady-state concentrations of apalutamide are achieved after 4 weeks of once-daily dosing and the mean accumulation ratio is approximately fivefold. Administration of apalutamide with a high-fat meal delays time to peak plasma concentration by approximately 2 hours but has no clinically important effects on peak plasma concentration or area under the concentration-time curve (AUC). Apalutamide is metabolized principally by cytochrome P-450 (CYP) isoenzymes 2C8 and 3A4 to form its major active metabolite, *N*-desmethylapalutamide, which exhibits antiandrogenic activity at one-third the potency of the parent drug in vitro. The contributions of CYP2C8 and 3A4 to the metabolism of apalutamide are approximately 58 and 13%, respectively, following a single dose and 40 and 37%, respectively, at steady state. Apalutamide and *N*-desmethylapalutamide account for 45 and 44%, respectively, of the total drug exposure following a single 240-mg dose of apalutamide.

Apalutamide and *N*-desmethylapalutamide are 96 and 95% bound, respectively, to plasma proteins; the extent of binding is independent of plasma concentration. Clearance of apalutamide is increased at steady state, suggesting that the drug may induce its own metabolism by CYP3A4. The mean steady-state half-life of apalutamide is approximately 3 days. Following oral administration of a single radiolabeled dose of apalutamide, 65% of the dose was recovered in urine (1.2% as unchanged drug and 2.7% as *N*-desmethylapalutamide) and 24% of the dose was recovered in feces (1.5% as unchanged drug and 2% as *N*-desmethylapalutamide).

Advice to Patients

Importance of reading the manufacturer's patient information.

For patients currently receiving gonadotropin-releasing hormone (GnRH) analog therapy, importance of continuing this therapy during apalutamide therapy.

Importance of advising patients to take apalutamide at the same time each day without regard to food and to swallow tablets whole. If a dose is missed, importance of taking the missed dose as soon as possible on the same day and taking the next dose at the regularly scheduled time on the following day. Extra tablets should not be taken to make up for a missed dose.

Risk of falls and fractures.

Risk of seizures. Importance of informing patients of the risk of engaging in activities where sudden loss of consciousness could cause serious harm to themselves or others. Importance of patients immediately informing their clinician if a seizure occurs.

Importance of patients notifying their clinician if a rash develops during apalutamide therapy.

Risk of fetal harm. Necessity of advising patients with female partners of childbearing potential to use effective methods of contraception during apalutamide therapy and for 3 months after the last dose of the drug. In addition, patients receiving the drug should be advised to use a condom during sexual encounters with pregnant women.

Importance of advising patients that apalutamide may impair male fertility and that they should not donate sperm during apalutamide therapy and for 3 months after the last dose of the drug.

Importance of informing clinicians of existing or contemplated concomitant therapy, including prescription and OTC drugs and dietary or herbal supplements, as well as any concomitant illnesses (e.g., seizures).

Importance of informing patients of other important precautionary information. (See Cautions.)

Overview® (see Users Guide). For additional information on this drug until a more detailed monograph is developed and published, the manufacturer's labeling should be consulted. It is *essential* that the manufacturer's labeling be consulted for more detailed information on usual cautions, precautions, contraindications, potential drug interactions, laboratory test interferences, and acute toxicity. For further information on the pharmacology of antineoplastic agents, resistance, and general principles in cancer chemotherapy, see the Antineoplastic Agents General Statement 10:00 at http://www.ahfsdruginformation.com. For further information on the handling of antineoplastic agents, see the ASHP Guidelines on Handling Hazardous Drugs at http://www.ahfsdruginformation.com.

Preparations

Distribution of apalutamide is restricted. (See Restricted Distribution under Dosage and Administration: General.)

Excipients in commercially available drug preparations may have clinically important effects in some individuals; consult specific product labeling for details.

Apalutamide

Oral

Tablets, film-coated	60 mg	**Erleada®**, Janssen