Starting and Staying on ERLEADA® (apalutamide)

A GUIDE FOR HEALTHCARE PROVIDERS AND PATIENT CARE TEAMS

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)

Please see Important Safety Information on page 16 and full Prescribing Information for ERLEADA®.

Johnson&Johnson

Help Your Patients
START AND STAY ON THERAPY

Erleada® (apalutamide) 60 mg tablets 240 mg tablet

Starting and staying on a medication can feel overwhelming for your patients. Janssen has resources to help you support your patients once you have made the clinical decision to prescribe ERLEADA®.

Janssen CarePath is your one source for access, affordability, and treatment support for your patients. Our dedicated Care Coordinator team supports the Janssen medications you prescribe. We can help make it easier for you and your patients to get the resources you both may need. Janssen CarePath helps verify insurance coverage for your patients, provides reimbursement information, helps find financial assistance options for eligible patients, and provides ongoing support to help patients start and stay on the ERLEADA® treatment that you prescribed.

TABLE OF CONTENTS

Information about your patient's insurance coverage, cost support options, and treatment support is given by service providers for Janssen CarePath. The information you get does not require you or your patient to use any Janssen product. Because the information we give you comes from outside sources, Janssen CarePath cannot promise the information will be complete. Janssen CarePath cost support is not for patients in the Johnson & Johnson Patient Assistance Foundation.

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.

Four Key Steps to HELP PATIENTS ACCESS MEDICATION

After the clinical decision has been made to prescribe ERLEADA®, the next step is to help your patients access their medication. Once you understand the overall process, it can be adapted to address the individual needs of your patients through various channels. In addition, Janssen CarePath can help you and your care team address a wide range of access and reimbursement challenges that may arise. Please see page 15 for more information.

To help you get started, we have broken the process down into 4 steps, each of which will be discussed on the following pages:

CONNECT › **COVERAGE** › **COST SHARE** › **CONTINUE CARE**

Talk to patients about their insurance

Get details about coverage and out-of-pocket (OOP) costs

Discuss cost sharing and financial assistance options

Identify ongoing support

PATIENTS CAN RECEIVE ERLEADA® VIA 2 OPTIONS

Specialty Pharmacy Provider (SPP)

— OR —

In-Office Dispensing Pharmacy (IODP)

IMPORTANT SAFETY INFORMATION (CONTINUED)
WARNINGS AND PRECAUTIONS (CONTINUED)

Cerebrovascular and Ischemic Cardiovascular Events (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.

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.

STEP 1:
CONNECT

As with any prescription medication, the first step in helping a patient start and stay on ERLEADA® is to gather important details and information. For example, does the patient receive benefits through a spouse? Does the insurer have a preferred or mandated SPP?

Asking such questions up front is important because patients may not always understand the details of their coverage, and may receive benefits from a number of sources, including:

- Commercial health plans
- Government-sponsored health plans (eg, Medicare, Medicaid, TRICARE, Department of Veterans Affairs)
- Retiree benefits

TWO IMPORTANT REMINDERS:

- **ERLEADA® is covered under the prescription benefit**
- **Be sure to ask patients if they have more than one source of insurance coverage (eg, spousal and supplemental coverage)**

Specialty Pharmacy Provider (SPP)

1. Office collects insurance information
2. Office forwards patient insurance information to SPP

In-Office Dispensing Pharmacy (IODP)[1]

1. Office collects insurance information
2. Office staff provides insurance information to the IODP

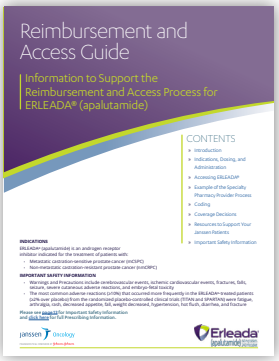
IMPORTANT SAFETY INFORMATION (CONTINUED)
WARNINGS AND PRECAUTIONS (CONTINUED)

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.

Please see Important Safety Information on page 16 and full Prescribing Information for ERLEADA®.

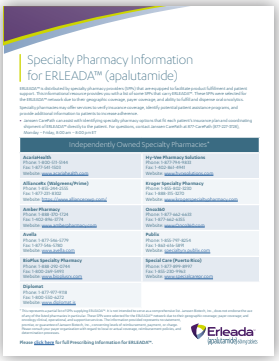
STEP 1:
CONNECT (continued)

RESOURCES



▸ Reimbursement and Access Guide

In this brochure you will find details about working with SPPs and Specialty Distributors (SDs), diagnosis codes for ERLEADA®, and other helpful information.



▸ Specialty Pharmacy Information for ERLEADA®

This resource contains contact information for SPPs and SDs currently authorized to distribute or sell ERLEADA®.

Resources shown are examples and are subject to change.

IMPORTANT SAFETY INFORMATION (CONTINUED)
WARNINGS AND PRECAUTIONS (CONTINUED)

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.

STEP 2:
COVERAGE

Erleada® (apalutamide) 60 mg tablets 240 mg tablet

After you have identified a patient's sources of insurance, the next step is to get the details about coverage and out-of-pocket (OOP) financial responsibilities. This process begins with a benefits investigation (BI), which can be handled by a Specialty Pharmacy Provider (SPP) within the ERLEADA® distribution network, your practice's In-Office Dispensing Pharmacy (IODP), or by Janssen CarePath. Once benefits have been verified, you can take the next steps toward helping a patient start and stay on ERLEADA®.

Janssen CarePath can help you with benefits investigation support, prior authorization support and status monitoring, information on reimbursement and the exceptions and appeals process, and prescription triage to SPPs.

Specialty Pharmacy Provider (SPP)

1. Healthcare provider (HCP) or Janssen CarePath submits prescription to SPP
2. SPP conducts benefits investigation (BI), verifies coverage, and determines patient OOP responsibility
3. SPP communicates PA requirements and other important information (eg, coverage and OOP responsibility) to HCP office
4. HCP completes PA paperwork and provides supporting documentation to SPP
5. SPP supports the PA process*

In-Office Dispensing Pharmacy (IODP)[1]

1. HCP sends prescription to IODP
2. IODP conducts BI, verifies coverage, and determines patient OOP responsibility
3. IODP initiates PA process

* SPP can also assist with exceptions requests and appeals (if necessary)

1. Egerton NJ. In-office dispensing of oral oncolytics: a continuity of care and cost mitigation model for cancer patients. *Am J Manag Care.* 2016;22(Suppl 4):S99-S103.

IMPORTANT SAFETY INFORMATION (CONTINUED)
WARNINGS AND PRECAUTIONS (CONTINUED)

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®.

STEP 2: COVERAGE (continued)

POTENTIAL CHALLENGES WITH PRIOR AUTHORIZATIONS (PAs)

PA denials may sometimes delay the time it takes for patients to access ERLEADA®, or even prevent patients from getting therapy. Common reasons for PA denials may include:

- Drug not on payer formulary
- Missing codes or documentation
- Desired use not consistent with payer coverage policy
- Medical necessity not established
- Step therapy requirements not met

Having your patient's complete medical history, specific diagnosis and diagnosis code, and rationale for treatment detailed in your request for coverage can help the approval process.

To assist your office with this process, we have created several checklists and resources for which links can be found on the next page. Download a Sample Letter of Medical Necessity and Sample Exception Letter for your office.

TIP: Janssen CarePath helps verify insurance coverage for your patients taking ERLEADA® and provides reimbursement information and status monitoring of PAs.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

Severe Cutaneous Adverse Reactions (continued) — 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)]*.

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)]*.

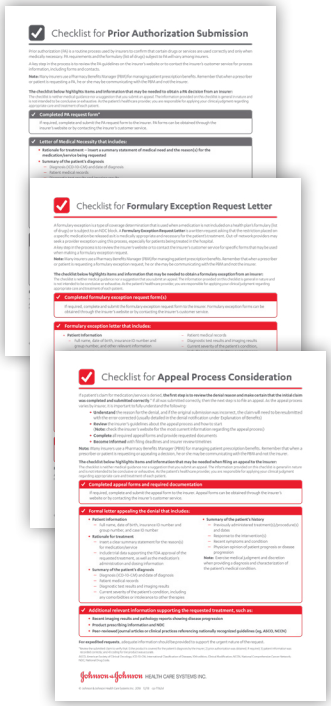
ADVERSE REACTIONS

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.

Erleada® (apalutamide) 60 mg tablets 240 mg tablet

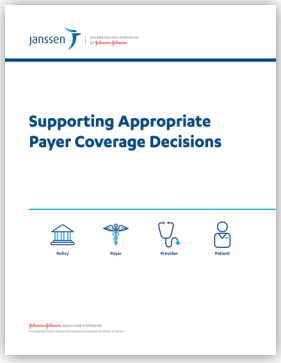
STEP 2:
COVERAGE (continued)

RESOURCES



- **Checklist for Prior Authorization Submission**
- **Checklist for Formulary Exception Request Letter**
- **Checklist for Appeal Process Consideration**

Use these checklists to keep track of best practices and documentation often required for PA submissions, exception requests, and appeals.



- **Supporting Appropriate Payer Coverage Decisions**

This brochure can help HCPs and care teams understand how to work with payers for coverage of medically necessary drug therapies, with a focus on PAs, coverage determinations (including exceptions), and appeals.

Resources shown are examples and are subject to change.

STEP 3:
COST SHARE

After your patient's prior authorization (PA) is approved, it will be time to discuss options for out-of-pocket (OOP) costs.

Janssen CarePath, the SPP network, or your practice's IODP may explore additional types of affordability support, depending on your patient's coverage.

Remember: It is helpful to discuss OOP costs with your patients. To do so, **consider using the checklist below as a guide.** You can also refer them to **Janssen CarePath** for assistance with affordability resources.

- ✓ **Patients with commercial insurance** may be eligible for the Janssen CarePath Savings Program (see next page)
- ✓ **Active military and retired veterans** may have additional VA or TRICARE benefits
- ✓ **Patients with Medicare or other government-sponsored insurance** *may* be eligible for a range of affordability support (see pages 11-13 for more details)
  - ✓ Medicare Part D Low-Income Subsidy (LIS), also known as "Extra Help"
  - ✓ State Pharmaceutical Assistance Programs (SPAPs)
  - ✓ Independent foundations*
  - ✓ The State Health Insurance Assistance Program (SHIP) for one-on-one counseling and support

* Independent co-pay assistance foundations have their own rules for eligibility. We have no control over these independent foundations and can only refer your patients to a foundation that supports their disease state. We do not endorse any particular foundation.

Specialty Pharmacy Provider (SPP)

1. SPP identifies potential patient assistance programs as needed
2. Your office assists with patient application/enrollment

In-Office Dispensing Pharmacy (IODP)[1]

1. Your staff helps to identify potential patient assistance programs and assists with application/enrollment as needed

Erleada® (apalutamide) 60 mg tablets 240 mg tablet

STEP 3:
COST SHARE (continued)

Janssen CarePath

Support for patients using commercial or private insurance to pay for medication

Janssen CarePath Savings Program for ERLEADA® can help eligible patients receive instant savings on their out-of-pocket medication costs for ERLEADA®. Depending on the patient's health insurance plan, savings may apply toward co-pay, co-insurance, or deductible. Your eligible patients will **pay $0 per month**. Maximum program benefit per calendar year shall apply. Not valid for patients using Medicare, Medicaid, or other government-funded programs to pay for their medications. Terms expire at the end of each calendar year and may change. Offer subject to change or discontinuance without notice. Restrictions, including monthly maximums, may apply. There is no income requirement. See program requirements at **Erleada.JanssenCarePathSavings.com**.

Express Enrollment site at **JanssenCarePathPortal.com/express** allows you to check eligibility and enroll patients in the Janssen CarePath Savings Program for ERLEADA® with no Business Associate Agreement (BAA) required. You will not have a Janssen CarePath account and you will not be able to view patients' Savings Program benefits until you create an account at **JanssenCarePathPortal.com.**

Creating an account on the Janssen CarePath Provider Portal at JanssenCarePathPortal.com allows providers to not only enroll eligible patients in the Janssen CarePath Savings Program but also manage patients' Savings Program benefits.

Patients can manage Savings Program benefits and more on their Janssen CarePath Account at MyJanssenCarePath.com

IMPORTANT SAFETY INFORMATION (CONTINUED)
ADVERSE REACTIONS (CONTINUED)

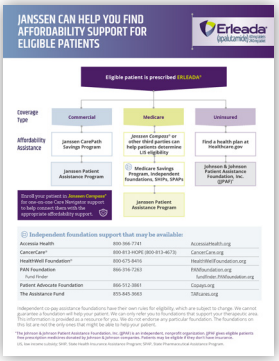
Laboratory Abnormalities — All Grades (Grade 3-4)

- **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%)

STEP 3:
COST SHARE (continued)

RESOURCES



▸ ERLEADA® Access Affordability Flashcard

This flashcard contains information about the support programs available to help patients start and stay on treatment.

▸ Janssen CarePath Savings Program

This brochure will help commercially insured patients understand benefits, eligibility, and enrollment for the Janssen CarePath Savings Program for ERLEADA®.

Resources shown are examples and are subject to change.

IMPORTANT SAFETY INFORMATION (CONTINUED)

ADVERSE REACTIONS (CONTINUED)

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®.

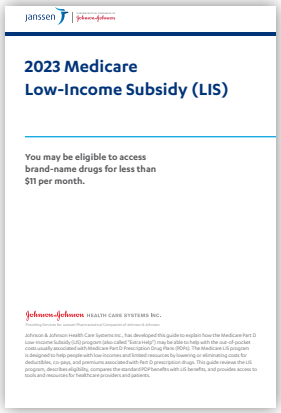
Hypothyroidism — In 2 randomized studies (SPARTAN and TITAN), hypothyroidism was reported for 8% of patients treated with ERLEADA® and 1.5% of patients treated with placebo based on assessments of thyroid-stimulating hormone (TSH) every 4 months. Elevated TSH occurred in 25% of patients treated with 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.

STEP 3:
COST SHARE (continued)

RESOURCES (continued)

▸ Know Your State

This interactive tool provides a range of state-specific information on access and affordability options.



▸ Extra Help With Prescription Drug Costs

This brochure helps your Medicare Part D patients understand the Low-Income Subsidy (Extra Help) program. Through the program, eligible patients may be able to receive significant discounts on prescription medications.

Resources shown are examples and are subject to change.

IMPORTANT SAFETY INFORMATION (CONTINUED)

DRUG INTERACTIONS

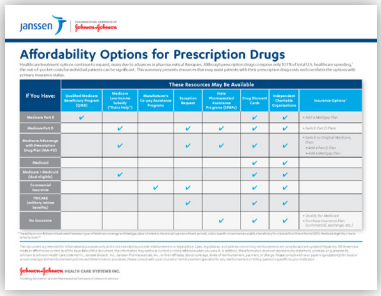
Effect of Other Drugs on ERLEADA® — Co-administration of a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties. No initial dose adjustment is necessary; however, reduce the ERLEADA® dose based on tolerability *[see Dosage and Administration (2.2)]*.

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.

STEP 3:
COST SHARE (continued)

RESOURCES (continued)


Affordability Options for Prescription Drugs

▸ Affordability Options for Prescription Drugs

This fact sheet provides at-a-glance information resources for patients, including those with commercial insurance, government-sponsored insurance, or patients who are underinsured.

▸ *Janssen Compass*® Personalized Support

Janssen Compass® is a free, personalized patient support program that can help your patients get started with their treatment and stay on track. Look to *Janssen Compass*® to help them navigate cost support options, as well as one-on-one guidance in learning about educational resources they need to feel confident on their Janssen therapy.

Resources shown are examples and are subject to change.

IMPORTANT SAFETY INFORMATION (CONTINUED)
DRUG INTERACTIONS (CONTINUED)

Effect of ERLEADA® on Other Drugs (continued)

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.

STEP 4:
CONTINUE CARE

The ultimate goal is to ensure patients receive the medications they need so they can start and stay on treatment. After your office, Janssen CarePath, or an SPP partner identifies sources of support for patient out-of-pocket (OOP) costs as needed, the SPP will coordinate delivery to your patient or your patient can pick up ERLEADA® through the IODP. Janssen CarePath is available to help patients with access challenges related to refills and adherence.

PARTNER WITH YOUR PATIENTS AT EACH STEP

Make sure the office is regularly keeping in touch with patients. Advise patients in advance that a pharmacy may be contacting them to obtain and confirm personal information to help with insurance authorizations and drug delivery, and inform patients to contact the office if they have any questions before providing information to a third party. The more patients understand about the process of obtaining ERLEADA®, the more they can share responsibility for their treatment. For example, patients:

- **Must answer calls from an SPP or your office to coordinate payment and delivery**
- **Need to know the name and contact information for the SPP**
- **May need to take an active role in applying for affordability support programs**

PATIENT COMMUNICATION IS KEY TO ENCOURAGING ADHERENCE

Encourage patients to contact their HCP, SPP, and/or IODP if they experience any obstacles to adhering to ERLEADA® exactly as prescribed (eg, difficulty with OOP costs or side effects). Patients will receive several important calls:

- **SPP or IODP will remind them to refill their prescription**
- **SPP or IODP will confirm refill and delivery or pick-up**

Specialty Pharmacy Provider (SPP)

1. Once patient OOP costs are paid, SPP coordinates shipment of ERLEADA®
2. SPP provides medication adherence support

In-Office Dispensing Pharmacy (IODP)[1]

1. Once patient OOP costs are paid, patient picks up ERLEADA® from IODP

JANSSEN CAREPATH PATIENT SUPPORT

Erleada® (apalutamide) 60 mg tablets 240 mg tablet

Janssen CarePath

Your one source for access, affordability, and treatment support for your patients

Access support to help navigate payer processes

Janssen CarePath helps verify insurance coverage for your patients taking ERLEADA® and provides reimbursement information.

Online benefits investigation and prior authorization support at **JanssenCarePathPortal.com**.

Affordability support to help your patients start and stay on the treatment you prescribe

Janssen CarePath can help you find out what affordability assistance may be available for your patients taking ERLEADA®.

Comprehensive Provider Portal to enroll eligible patients in the Janssen CarePath Savings Program and more at **JanssenCarePathPortal.com**.

Express Enrollment for Savings Program for ERLEADA® at **JanssenCarePathPortal.com/express**.

Call Janssen CarePath at 877-CarePath (877-227-3728), Monday-Friday, 8:00 AM to 8:00 PM ET. Multilingual phone support available.

Sign Up or log in to the Provider Portal at JanssenCarePathPortal.com, where you can request and review benefits investigations, enroll eligible patients in the Janssen CarePath Savings Program and view Savings Program transactions as requested by the patient.

Visit JanssenCarePath.com.

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 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.

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)].*

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)].*

(continued on next page)

IMPORTANT SAFETY INFORMATION (CONTINUED)

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 the full Prescribing Information for ERLEADA®.

cp-50507v6

Johnson&Johnson

Erleada® (apalutamide) 60 mg tablets 240 mg tablet

Visit erleadahcp.com