As soon as you diagnose mCSPC or nmCRPC

START EARLY WITH ERLEADA® (apalutamide)

TO PUSH BACK ON PROGRESSION

START EARLY WITH ERLEADA® TO GIVE YOUR PATIENTS A CHANCE TO LIVE LONGER

PROVEN EFFICACY[1,2]

TITAN study in mCSPC (dual primary endpoint)*:

FIRST AND ONLY

AR inhibitor to achieve a **35%** reduction in the risk of death in a registration trial in mCSPC

- (Median OS: NR vs 52.2 months; HR=0.65; 95% CI: 0.53, 0.79; *P*<0.0001; median follow-up time for final analysis: 44.0 months)[†2]
- (Median OS: NE vs NE; HR=0.67; 95% CI: 0.51, 0.89; *P*=0.0053; median follow-up time for primary analysis: 22.7 months)

SPARTAN study in nmCRPC (primary endpoint)[‡]:

FIRST AND ONLY

AR inhibitor to improve median MFS by **2 YEARS** in nmCRPC

- (40.5 months vs 16.2 months; HR=0.28; 95% CI: 0.23, 0.35; *P*<0.0001; median follow-up time for primary analysis: 20.3 months)[1,4]

TITAN study in mCSPC (dual primary endpoint)*:

ERLEADA® + ADT reduced the risk of radiographic progression or death by **52%** vs placebo + ADT

- (Median rPFS NE vs 22.1 months; HR=0.48; 95% CI: 0.39, 0.60; *P*<0.0001; median follow-up time for primary analysis: 22.7 months)[1,3]

SPARTAN study in nmCRPC (secondary endpoint)[‡]:

FIRST AND ONLY

therapy to improve median OS by **14 MONTHS** in nmCRPC

- (73.9 months; [6.2 years] vs 59.9 months [5 years]; HR=0.78; 95% CI: 0.64, 0.96; *P*=0.0161; median follow-up time for final analysis: 52.0 months)[1,5]

ESTABLISHED SAFETY PROFILE[1]

- In 2 pivotal trials that included a total of more than 2000 patients, the rate of serious adverse reactions with ERLEADA® + ADT was comparable with placebo + ADT[1]
  - TITAN Study: 20% ERLEADA® + ADT vs 20% placebo + ADT[1]
  - SPARTAN Study: 25% ERLEADA® + ADT vs 23% placebo + ADT[1]

NO NEGATIVE IMPACT TO HRQoL

(exploratory endpoint)[§6,7]

- In the TITAN study, HRQoL was maintained with ERLEADA® + ADT after a median follow-up of 44 months. Analysis of change from baseline in the FACT-P total score showed no substantial between-group differences[2]
- In the SPARTAN study, HRQoL was maintained with ERLEADA® + ADT after a median follow-up of 52 months. In patients receiving placebo + ADT, HRQoL declined after approximately 1 year[8]

BROAD ACCESS[9]

ERLEADA® is covered for 95% of Medicare Part D patients and 78% of commercial patients.[‖,9,10]

*All patients who enrolled in the TITAN study started ADT for mSCPC ≤6 months prior to randomization.[3]

[†]**TITAN final analysis data are not currently reported in the ERLEADA® Prescribing Information.**

[‡]In the SPARTAN study, conventional imaging (technetium-99m bone scans and CT scans) was used to confirm that patients were non-metastatic at screening for inclusion. Patients with pelvic lymph nodes <2 cm in short axis (N1) located below the iliac bifurcation at screening were allowed in the study. All patients in SPARTAN had a PSA doubling time ≤10 months in study entry.[1,4]

[§]The HRQoL analyses are not in the ERLEADA® Prescribing Information.

[‖]Prior authorization to label required for most plans.

ADT = androgen deprivation therapy; AR = androgen receptor; CI = confidence interval; CT = computed tomography; FACT-P = Functional Assessment of Cancer Therapy-Prostate; HR = hazard ratio; HRQoL = health-related quality of life; MFS = metastasis-free survival; mCSPC = metastatic castration-sensitive prostate cancer; MMIT = Managed Markets Insights & Technology; NE = non-estimable; nmCRPC = non-metastatic castration-resistant prostate cancer; NR = not reached; OS = overall survival; PSA = prostate-specific antigen; rPFS = radiographic progression-free survival; SPARTAN = Selective Prostate Androgen Receptor Targeting with ARN-509; TITAN = Targeted Investigational Treatment Analysis of Novel Antiandrogen.

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 include cerebrovascular and ischemic cardiovascular events, fractures, falls, seizure, and embryo-fetal toxicity
- 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

Please see Important Safety Information inside and the full Prescribing Information for ERLEADA®.

Erleada® (apalutamide) 60 mg tablets

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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 4% of patients treated with ERLEADA® and 3% of patients treated with placebo. In a randomized study (TITAN) in patients with mCSPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA® and 2% of patients treated with placebo. Across the SPARTAN and TITAN studies, 5 patients (0.5%) 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 4.7% of patients treated with ERLEADA® and 0.8% 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.

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

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% (2%), placebo 21% (2%)
- **Chemistry** — In the TITAN study: hypertriglyceridemia ERLEADA® 17% (3%), placebo 12% (2%). In the SPARTAN study: hypercholesterolemia ERLEADA® 76% (0.1%), placebo 46% (0%); hyperglycemia ERLEADA® 70% (2%), placebo 59% (1%); hypertriglyceridemia ERLEADA® 67% (2%), placebo 49% (0.8%); hyperkalemia ERLEADA® 32% (2%), 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®.

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IMPORTANT SAFETY INFORMATION (CONT´D)

Hypothyroidism — In 2 randomized studies (SPARTAN and TITAN), hypothyroidism was reported for 8% of patients treated with ERLEADA® and 2% 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.

cp-50507v3

Please click to see the full Prescribing Information for ERLEADA®.

References: 1. ERLEADA® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Chi KN, Chowdhury S, Bjartell A, et al. Apalutamide in patients with metastatic, castration-sensitive prostate cancer: final survival analysis of the randomized, double-blind, phase III TITAN study [published online April 29, 2021]. *J Clin Oncol*. doi.org/10.1200/JCO.20.03488 **3.** Chi KN, Agarwal N, Bjartell A, et al; for the TITAN Investigators. Apalutamide for metastatic, castration-sensitive prostate cancer. *N Engl J Med*. 2019;381(1):13-24. **4.** Smith MR, Saad F, Chowdhury S, et al; for the SPARTAN Investigators. Apalutamide treatment and metastasis-free survival in prostate cancer. *N Engl J Med*. 2018;378(15):1408-1418. **5.** Smith MR, Saad F, Chowdhury S, et al. Apalutamide and overall survival in prostate cancer. *Eur Urol.* 2021;79(1):150-158. **6.** Agarwal N, McQuarrie K, Bjartell A, et al; TITAN Investigators. Health-related quality of life after apalutamide treatment in patients with metastatic castration-sensitive prostate cancer (TITAN): a randomised, placebo-controlled, phase 3 study. *Lancet Oncol*. 2019;20(11):1518-1530. **7.** Saad F, Cella D, Basch E, et al. Effect of apalutamide on health-related quality of life in patients with non-metastatic castration-resistant prostate cancer: an analysis of the SPARTAN randomised, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2018;19(10):1404-1416. **8.** Oudard S, Hadaschik B, Saad F, et al. Health-related quality of life at final analysis of the SPARTAN study of apalutamide vs placebo in patients with nonmetastatic castration-resistant prostate cancer receiving androgen deprivation therapy. Poster presented at: ESMO Virtual Congress; September 18-22, 2020. **9.** MMIT; February 2021. **10.** Data on file. Janssen Biotech, Inc. Date of data July 2021. Date information was collected June 2021.

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