Erleada® (apalutamide) tablets

ERLEADA® is indicated for the treatment of patients with metastatic castration-sensitive prostate cancer (mCSPC).

mCSPC

In the TITAN trial, treatment with ERLEADA® + ADT:

reduced the instantaneous risk of death (OS) by 33% vs. placebo + ADT in patients with mCSPC[1,2]*
(HR 0.67; 95% CI: 0.51-0.89; *p*=0.0053) (dual primary endpoint)
Number of events: ERLEADA® + ADT = 83/525; placebo + ADT = 117/527

reduced the risk of radiographic progression or death (rPFS) by 52% vs. placebo + ADT[1,2]*
(HR 0.48; 95% CI: 0.39-0.60; *p*<0.0001) (dual primary endpoint)
Number of events: ERLEADA® + ADT = 134/525; placebo + ADT = 231/527

» Apalutamide recommendation in the Canadian Urological Association guidelines

Apalutamide is one recommended treatment option for men with mCSPC regardless of volume of disease

(Level of evidence 1, Strong recommendation)[5]

Clinical Use:
ERLEADA® has not been studied during pregnancy or in children.

Contraindications:
- Women who are or may be pregnant.

Relevant Warnings and Precautions:
- Assess for active cardiac disease before and during treatment with ERLEADA®.
- Monitor patients with known history of QT prolongation, risk factors for torsades de pointes, or taking medications known to prolong QT interval.
- Assess patients for risk of fracture and fall.
- Ischemic cerebrovascular events.
- Patients with a history of stroke.
- Permanently discontinue in patients who develop a seizure during treatment.
- May harm unborn baby or increase risk for loss of pregnancy. Use effective contraception with female partners of reproductive potential during treatment and for 3 months after the last dose of ERLEADA®. Male patients should not donate sperm during treatment and for 3 months after the last dose of ERLEADA®.
- Potential to impair fertility in males based on animal studies.
- Monitor TSH during treatment for hypothyroidism.
- Monitor for disease progression radiographically in addition to serum PSA.
- ERLEADA® is not indicated for use in women.

For More Information:
Consult the Product Monograph at janssen.com/canada/products for important information regarding adverse reactions, drug interactions and dosing instructions which have not been discussed in the piece. The Product Monograph is also available by calling 1-800-567-3331 or 1-800-387-8781.

ERLEADA® is indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC).
ERLEADA® has not been studied in patients with nmCRPC at low risk of developing metastases. The benefit and risk profile in these patients is unknown.

nmCRPC

In the SPARTAN trial, treatment with ERLEADA® + ADT:

significantly reduced the instantaneous risk of death or metastasis (MFS) by 70% vs. placebo + ADT[3]
(HR 0.30; 95% CI: 0.24-0.36; *p*<0.0001)
Number of events: ERLEADA® + ADT = 209/806; placebo + ADT = 210/401

significantly reduced the instantaneous risk of death (OS) by 22% vs. placebo + ADT[1,4†] (HR 0.78; 95% CI: 0.64-0.96; *p*=0.0161) (secondary endpoint, final analysis)
Number of events: ERLEADA® + ADT = 274/806; placebo + ADT = 154/401

significantly improved progression-free survival (PFS) vs. placebo + ADT[1,4†] (HR 0.30; 95% CI: 0.25-0.36; *p*<0.0001) (secondary endpoint, final analysis)
Number of events: ERLEADA® + ADT = 220/806; placebo + ADT = 219/401

The final analysis of overall survival was conducted 32 months after the primary analysis of MFS. At the time of primary analysis, patients treated with ADT alone were given the opportunity to cross-over to treatment with ERLEADA® at the time of unblinding. After unblinding, 19% of the randomized placebo population crossed over to ERLEADA®. Patients who had crossed over had a median treatment duration of 26 months with ERLEADA® treatment.

» Apalutamide recommendation in the Canadian Urological Association guidelines

Apalutamide is one treatment option that should be offered to men with high-risk nmCRPC, defined as a PSA doubling time (PSADT) of less than 10 months, with an estimated life expectancy of greater than 5 years

(Level of evidence 1, Strong recommendation)[6]

ADT=androgen deprivation therapy; TTICC=time to initiation of cytotoxic chemotherapy; MFS=metastasis free survival; TTM=time to metastasis; PFS=progression free survival; TTSP=time to symptomatic progression; BICR=blinded independent central review.

* TITAN was a randomized, double-blind, placebo-controlled, clinical trial in which 1052 patients with mCSPC were randomized (1:1) to receive either ERLEADA® orally at a dose of 240 mg once daily (n=525) or placebo daily (n=527). All patients received androgen deprivation therapy (ADT) as concomitant GnRH analog or had prior bilateral orchiectomy. Patients were stratified by Gleason score at diagnosis, prior docetaxel use, and region of the world. Patients with both high- and low-volume and high- and low-risk mCSPC were eligible for the study.
The dual primary endpoints of the study were overall survival (OS) and radiographic progression-free survival (rPFS). rPFS is defined as the duration from the date of randomization to the date of first documentation of radiographic progressive disease (progression of soft tissue lesions as per modified RECIST 1.1 criteria or ≥2 bone lesions on bone scan compared to baseline lesions) or death due to any cause, whichever comes first. Median follow-up time was 22.7 months. The median treatment duration was 20.5 months in the ERLEADA® arm and 18.3 months in the placebo + ADT arm. At the time of analysis, 66% patients in the ERLEADA® arm and 46% of patients in the placebo arm were continuing study treatment. Median overall survival was not estimable in either arm.

† SPARTAN: Phase III, randomized, double-blind, placebo-controlled study in patients with nmCRPC (N=1207). Patients were randomized 2:1 to receive ERLEADA® 240 mg OD or placebo, both in combination with ADT (GnRH analog or bilateral orchiectomy). The primary endpoint was metastasis-free survival, defined as the time from randomization to the time of first evidence of blinded-independent-central-review-confirmed bone or soft tissue distant metastasis or death due to any cause, whichever occurred first.
The final analysis of OS and TTICC was conducted 32 months after the primary analysis of MFS, TTM, PFS and TTSP. At the time of primary analysis, patients treated with ADT alone were given the opportunity to cross-over to treatment with ERLEADA® at the time of unblinding. After unblinding, 19% of the randomized placebo population crossed over to ERLEADA®. Patients who had crossed over had a median treatment duration of 26 months with ERLEADA® treatment.

‡ Time to metastasis was defined as the time from randomization to the time of first evidence of BICR-confirmed radiographically detectable metastasis.

References:
1. ERLEADA® Product Monograph. Janssen Inc. July 6, 2021. **2.** Chi KN, *et al.* Apalutamide for metastatic, castration-sensitive prostate cancer. *N Engl J Med* 2019;381(1):13-24. **3.** Smith MR, *et al.* Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer. *N Engl J Med* 2018;378(15):1408-18. **4.** Smith MR, *et al.* Apalutamide and Overall Survival in Prostate Cancer. *Eur Urol* 2021;79:150-59. **5.** So AI, *et al.* Canadian Urological Association-Canadian Urologic Oncology Group guideline on metastatic castration-naïve and castration-sensitive prostate cancer. *Can Urol Assoc J* 2020;14(2):17-23. **6.** Saad F, *et al.* 2019 Canadian Urological Association (CUA)-Canadian Uro Oncology Group (CUOG) guideline: Management of castration-resistant prostate cancer (CRPC). *Can Urol Assoc J* 2021;15(2):E81-9.

Janssen Inc. 19 Green Belt Drive | Toronto, Ontario M3C 1L9
www.janssen.com/canada | CP-247986E

MEMBER OF INNOVATIVE MEDICINES CANADA
REVIEWED BY PAAB
Janssen PHARMACEUTICAL COMPANIES OF Johnson & Johnson