J-C Health Care Ltd.

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אוקטובר 2021

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

Erleada, Film Coated Tablets 162-84-35698-00

ברצוננו להביא לידיעתכם את העדכונים בעלון לרופא של התכשיר (העלון לצרכן נותר ללא שינוי)

הרשום להתוויות:

Erleada is indicated in adult men for the treatment of

- Metastatic hormone sensitive prostate cancer (mHSPC) in combination with androgen derivation therapy (ADT)
- Non-metastatic castration-resistant prostate cancer (nm-CRPC)

השינויים המהותיים בעלון לרופא מופיעים בסעיפים הבאים:

7.5 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 ~~*[see Clinical Pharmacology (13.1)].*~~ In an animal reproduction study, oral administration of apalutamide to pregnant rats during and after organogenesis resulted in fetal abnormalities and embryo-fetal lethality at maternal exposures ≥ 2 times the human clinical exposure (AUC) at the recommended dose. 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 (10.1, 10.3) and Clinical Pharmacology (13.1)]*.

[…]

10 USE IN SPECIFIC POPULATIONS

10.1 Pregnancy

Risk Summary

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 *[see Clinical Pharmacology (13.1)]*. There are no ~~human~~available data on ~~the use of~~ ERLEADA use in pregnant women~~. ERLEADA is not indicated for use in females, so~~ to inform a drug-associated risk. In an animal reproduction study, oral administration of apalutamide to pregnant rats during and after organogenesis resulted in fetal abnormalities and embryo-fetal ~~developmental toxicology studies were not conducted with apalutamide.~~lethality at maternal exposures ≥ 2 times the human clinical exposure (AUC) at the recommended dose *(see Data)*.

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Data

Animal Data

In a pilot embryo-fetal developmental toxicity study in rats, apalutamide caused developmental toxicity when administered at oral doses of 25, 50 or 100 mg/kg/day throughout and after the period of organogenesis (gestational days 6-20). Findings included embryo-fetal lethality (resorptions) at doses ≥50 mg/kg/day, decreased fetal anogenital distance, misshapen pituitary gland, and skeletal variations (unossified phalanges, supernumerary short thoracolumbar rib(s), and small, incomplete ossification, and/or misshapen hyoid bone) at ≥25 mg/kg/day. A dose of 100 mg/kg/day caused maternal toxicity. The doses tested in rats resulted in systemic exposures (AUC) approximately 2, 4 and 6 times, respectively, the AUC in patients.

[…]

14 NONCLINICAL TOXICOLOGY

14.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

~~Long-term animal studies have not been conducted to evaluate the carcinogenic potential of apalutamide.~~ Oral administration of apalutamide to male rasH2 transgenic mice for 6 months did not result in increased incidence of neoplasms at doses up to 30 mg/kg/day.

Apalutamide did not induce mutations in the bacterial reverse mutation (Ames) assay and was not genotoxic in either *in vitro* chromosome aberration assay or the *in vivo* rat bone marrow micronucleus assay or the *in vivo* rat Comet assay.

[…]

העלון לרופא נשלח לפרסום במלואו למאגר התרופות שבאתר משרד הבריאות. כמו כן, ניתן לקבלו מודפס בפניה אלינו לטלפון 09-9591111 .

בברכה,

צפריר כהן

רוקח ממונה