08/2026

Epidiolex
אפידיולקס

CANNABIDIOL 100MG/1ML
Solution

רופא/ה, רוקח/ת נכבד/ה,
חברת ניאופרם בע"מ מבקשת להודיע על עדכון העלונים לרופא ולצרכן של התכשיר שבנדון. העלונים עודכנו בתאריך 08/2026.

ההתוויה הרשומה ביום בישראל לתכשיר:
Epidiolex is indicated for use as adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), or tuberous sclerosis complex (TSC) in patients 1 year of age and older.

מקראה לעדכונים המסומנים:
מידע שהוסר -מסומן בקו אדום חוצה ~~XXX~~
תוספת -כתב **כחול**

להלן מתוארים העדכונים העיקריים בעלונים לרופא ולצרכן, בעלונים קיימים עדכונים נוספים.

6.1 Clinical Trials Experience
(…)
Increases in Creatinine
EPIDIOLEX can cause elevations in serum creatinine. ~~**The mechanism has not yet been determined.**~~ In controlled studies in healthy adults and in patients with LGS, DS, and TSC, an increase in serum creatinine of approximately 10% was observed within 2 weeks of starting EPIDIOLEX. The increase was reversible in healthy adults. Reversibility was not assessed in studies in LGS, DS, or TSC. **Results of another study in healthy adults demonstrate that the increases in serum creatinine noted with EPIDIOLEX are not due to a reduction in glomerular filtration rate *[see Clinical Pharmacology (11.2)]*.**

8.1 Pregnancy
(…)
Animal Data
Oral administration of cannabidiol (0, 75, 150, or 250 mg/kg/day) to pregnant rats throughout the period of organogenesis resulted in embryofetal mortality at the highest dose tested. There were no other drug related maternal or developmental effects. The highest no-effect dose for embryofetal toxicity in rats was associated with maternal plasma cannabidiol exposures (AUC) approximately 16 and ~~**9**~~ **13** times that in humans at the **maximum** recommended human doses (**M**RHD) of 20 and 25 mg/kg/day, respectively.

Oral administration of the major human cannabidiol metabolite, 7-COOH-CBD (0, 25, 50 or 100 mg/kg/day), to pregnant rats throughout the period of organogenesis resulted in embryofetal malformations and variations at the highest dose tested, which was not maternally toxic. The highest no effect dose for embryofetal developmental toxicity in rats (50 mg/kg/day) was associated with maternal plasma 7-COOH-CBD exposures (AUC) approximately 5 and 4 times that in humans at the MRHDs of 20 and 25 mg/kg/day cannabidiol, respectively.

(…)
Oral administration of 7-COOH-CBD (0, 20, 40, or 75 mg/kg/day) to rats throughout pregnancy and lactation resulted in adverse effects on neurobehavioral function (locomotor activity) in offspring when tested in adulthood at the mid and high doses, and on reproductive function (increased preimplantation loss) in offspring at all doses. The lowest dose tested, a no-effect dose for pre- and postnatal developmental toxicity in rats (20 mg/kg/day), was associated with maternal plasma 7-COOH-CBD exposures approximately 2 times that in humans at both MRHDs of 20 or 25 mg/kg/day cannabidiol.

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8.3 Pediatric Use

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Juvenile Animal Data

Administration of cannabidiol (subcutaneous doses of 0 or 15 mg/kg on Postnatal Days (PNDs) 4-6 followed by oral administration of 0, 100, 150, or 250 mg/kg on PNDs 7-77) to juvenile rats for 10 weeks resulted in increased body weight, delayed male sexual maturation, neurobehavioral effects (decreased locomotor activity and auditory startle habituation), increased bone mineral density, and liver hepatocyte vacuolation. A no-effect dose was not established. The lowest dose causing developmental toxicity in juvenile rats (15 sc/100 po mg/kg) was associated with cannabidiol exposures (AUC) approximately ~~15 and 8~~ **4** times that in humans at ~~the~~ **both M**RHDs of 20 and 25 mg/kg/day~~, respectively~~.

Administration of the major human cannabidiol metabolite 7-COOH-CBD (0, 20, 40, or 80 mg/kg/day) to juvenile rats by subcutaneous injection on PNDs 4-6 followed by oral gavage on PNDs 7-77, for a total of 10 weeks, resulted in mortality, ophthalmic abnormalities, and accelerated female sexual maturation at the mid and high doses, and long-term neurobehavioral (increased locomotor activity, decreased auditory startle response habituation and prepulse inhibition, delayed maze learning) and reproductive functional impairment (disrupted estrous cyclicity, decreased sperm concentration and increased abnormal sperm; decreased mating, fertility, and fecundity indices; increased preimplantation loss), decreased brain weight, and decreased bone density at the high dose. The no-effect dose for developmental toxicity in juvenile rats (20 mg/kg/day) was associated with 7-COOH-CBD exposures (AUC) that were approximately equivalent to that in humans at the MRHDs of 20 and 25 mg/kg/day.

11.2 Pharmacodynamics

Cardiac Electrophysiology

(…)

Effect of EPIDIOLEX on Measured Glomerular Filtration Rate (mGFR)

In a dedicated study in healthy subjects (N=39), EPIDIOLEX (7.5 mg/kg twice daily for 7 days) had no effect on the mGFR and mGFR normalized for body surface area (BSA), as determined by the clearance of probe drug iohexol (5 mL, IV infusion) following EPIDIOLEX administration versus baseline.

In this study, consistent with historic observations [see Adverse Reactions (6.1)], increases in serum creatinine and corresponding decreases in estimated GFR (using a combined serum creatinine- and cystatin C-based estimating equation) and 24-hour urinary creatinine clearance (CLcr) of 5% and 10%, respectively, were seen.

The results of this study demonstrate that EPIDIOLEX did not affect mGFR; therefore, the increase in serum creatinine observed with administration of EPIDIOLEX is not due to a reduction in glomerular filtration rate.

11.3 Pharmacokinetics

(…)

After repeat dosing, the active metabolite of cannabidiol, 7-OH-CBD, has a 38% lower AUC than the parent drug. The 7-OH-CBD metabolite is converted to 7 COOH-CBD, which has an approximately 40 fold higher AUC than the parent drug. Based on **two mouse** ~~preclinical~~ models of **acute** seizure, the 7-OH-CBD metabolite is **anticonvulsant in both models and** ~~active; however, the~~ 7 COOH-CBD ~~metabolite is not active~~ **is anticonvulsant in one model. The relevance of these findings to human epilepsy is unknown**.

12.1 Carcinogenesis and Mutagenesis

Carcinogenesis

In a carcinogenicity study in mice, oral administration of cannabidiol (0 [water], 0 [vehicle], 30, 100, or 300 mg/kg/day) for 2 years resulted in an increased incidence of hepatocellular adenomas in male mice at the highest dose tested. At the mid dose (100 mg/kg/day), plasma exposures (AUC) were approximately ~~5~~ **2** and ~~3~~ **1** times that at the **maximum** recommended human doses (**M**RHDs) of 20 and 25 mg/kg/day, respectively.

~~The carcinogenic potential of cannabidiol has not been assessed in rats~~ In a carcinogenicity study in rats, oral administration of cannabidiol (0 [water], 0 [vehicle], 15, 50, and 150 mg/kg/day) for 2 years, no statistically significant increases in tumor incidences were observed. At the high dose (150 mg/kg/day), the plasma exposures (AUC) were approximately 12.5 and 10 times that at the MRHDs of 20 and 25 mg/kg/day, respectively.

Mutagenesis

Cannabidiol was negative for genotoxicity in in vitro (Ames) and in vivo (rat Comet and bone marrow micronucleus) assays. **The cannabidiol metabolite 7-COOH-CBD was negative for genotoxicity in in vitro (Ames) and in vivo (rat Comet and bone marrow micronucleus) assays. The metabolite 7-OH-CBD was negative for genotoxicity in in vitro (Ames and mammalian cell [human lymphocyte] chromosomal aberration) assays and in vivo (rat micronucleus) assays.**

17 MANUFACTURER

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למידע נוסף יש לעיין בעלונים לרופא ולצרכן המעודכנים אשר נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות.
כמו כן, ניתן לקבל את עלוני התכשיר מודפסים על ידי פניה לבעל הרישום: ניאופרם בע"מ, ת.ד. 7063, פתח תקווה 4917001.
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בברכה
עוז וולך, רוקח/ת ממונה של בעל הרישום