תאריך : יוני 2018

הנדון: Flolan Infusion of Epoprostenol 500mcg, 1500mcg
פלולן אפופרוסטנול 500 מק"ג, 1500 מק"ג לעירוי
Epoprostenol (As sodium) 500 mcg, 1500 mcg / vial
Powder for solution for infusion

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

חברת גלקסוסמיתקליין ישראל בע"מ (GSK) מבקשת להודיע על עדכון העלון לרופא של
Flolan Infusion of Epoprostenol 500mcg, 1500mcg

- **ההתוויה הרשומה לתכשיר בישראל:**

Flolan is indicated for the long-term intravenous treatment of primary pulmonary hypertension and pulmonary hypertension associated with the scleroderma spectrum of disease in NYHA class III and class IV patients who do not respond to conventional therapy.

- **עדכונים מהותיים נעשו בסעיפים הבאים בעלון לרופא:**

Carcinogenesis, Mutagenesis, Impairment of Fertility

…

~~Fertility was not impaired in rats given FLOLAN by subcutaneous injection at doses up to 100 mcg/kg per day [600 mcg/m2 per day, 2.5 times the recommended human dose (4.6 ng/kg per minute or 245.1 mcg/m2 per day, IV) based on body surface area]~~

In a fertility/postnatal development study, epoprostenol sodium was administered subcutaneously to female rats for 2 weeks prior to mating through weaning and to male rats for 60 days prior to and through mating at an adult toxic dose of up to 100 mcg/kg/day (600 mcg/m2/day, 2.5 times the MRHD based on body surface area). There was no effect on fertility in female or male rats.

Pregnancy

~~Pregnancy Category B. Reproductive studies have been performed in pregnant rats and rabbits at doses up to 100 mcg/kg per day (600 mcg/m2 per day in rats, 2.5 times the recommended human dose, and 1180 mcg/m2 per day in rabbits, 4.8 times the recommended human dose based on body surface area) and have revealed no evidence of impaired fertility or harm to the fetus due to FLOLAN. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.~~

Risk Summary

Limited published data from case series and case reports have not established an association with FLOLAN and major birth defects, miscarriage or adverse maternal or fetal outcomes when FLOLAN is used during pregnancy. There are risks to the mother and fetus from untreated pulmonary arterial hypertension (see Clinical Considerations). In animal reproduction studies, pregnant rats and rabbits received epoprostenol sodium during organogenesis at exposures of 2.5 and 4.8 times the maximum recommended human dose (MRHD), respectively, and there was no effect on the fetus (see Data).

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk: Pregnant women with untreated pulmonary arterial hypertension are at risk for heart failure, stroke, preterm delivery, and maternal and fetal death.

Data

Animal Data: Embryo-fetal development studies have been performed in rats and rabbits during organogenesis. Epoprostenol sodium doses up to 100 mcg/kg/day, a dose that was maternally toxic in rabbits but not in rats, (600 mcg/m2/day in rats, 2.5 times the MRHD, and 1,180 mcg/m2/day in rabbits, 4.8 times the MRHD based on body surface area), had no effect on the fetus.

In a postnatal development study, epoprostenol sodium was administered subcutaneously to female rats for 2 weeks prior to mating through weaning and to male rats for 60 days prior to and through mating at a male and female toxic dose of up to 100 mcg/kg/day (600 mcg/m2/day, 2.5 times the MRHD based on body surface area). There was no effect on growth and development of the offspring.

Lactation ~~Nursing Mothers:~~

~~It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when FLOLAN is administered to a nursing woman.~~

Risk Summary

There are no data on the presence of epoprostenol in either human or animal milk, the effects on the breastfed infant, or the effect on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for FLOLAN and any potential adverse effects on the breastfed child from epoprostenol or from the underlying maternal condition

מקרא לעדכונים המסומנים:

תוספת החמרה - כתב **כחול** - מסומן בצהוב מרקר

תוספת - כתב **כחול**

טקסט שהוסר - ~~אדום~~ עם קו

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://www.old.health.gov.il/units/pharmacy/trufot/index.asp?safa=h וניתן לקבלו מודפס על-ידי פניה לחברת גלקסוסמיתקליין רח' בזל 25 פתח תקוה בטלפון: 03-9297100.

בברכה,

שרית רוזן

רוקחת ממונה