אוגוסט 2020

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

הנדון: FOSALAN ONCE-WEEKLY 70mg
פוסאלאן פעם בשבוע 70 מ"ג

Dosage Form: Tablets
Composition: Alendronate (as sodium) 70mg

חברת מרק שארפ ודוהם ישראל (MSD) מבקשת ליידע על עדכון העלונים לרופא ולצרכן של Fosalan OW 70mg.

להלן לשון ההתוויה המאושרת לתכשיר:
Fosalan is indicated for the treatment of osteoporosis in postmenopausal women to prevent fractures, including those of the hip and spine (vertebral compression fractures). Treatment to increase bone mass in men with osteoporosis.

למידע מלא ולהוראות מתן מפורטות, יש לעיין בעלון לרופא המאושר על ידי משרד הבריאות.

טקסט מהותי שהתווסף מודגש בקו תחתון.

עדכונים מהותיים בעלון לרופא:
הפרקים הבאים עברו עידכון ביחס למידע על הריון והנקה: 8.1-Pregnancy, 8.2- Lactation

8.1 Pregnancy
~~*Pregnancy Category C:*~~

Risk Summary

~~There are no studies~~ Available data on the use of FOSALAN in pregnant women ~~FOSALAN should be used during~~ are insufficient to inform a drug-associated risk of adverse maternal or fetal outcomes. Discontinue FOSALAN when pregnancy is recognized. ~~Pregnancy only if the potential benefit justifies the potential risk to the mother and fetus.~~

In animal reproduction studies, daily oral administration of alendronate to rats from before mating through the end of gestation or lactation showed decreased postimplantation survival and decreased pup body weight gain starting at doses equivalent to less than half of the highest recommended 40 mg clinical daily dose (based on body surface area, mg/m2). Oral administration of alendronate to rats during organogenesis resulted in reduced fetal ossification starting at doses 3 times the 40 mg clinical daily dose. No similar fetal effects were observed in pregnant rabbits dosed orally during organogenesis at doses equivalent to approximately 10 times the 40 mg clinical daily dose.

Delayed or failed delivery of offspring, protracted parturition, and late pregnancy maternal and fetal deaths due to maternal hypocalcemia occurred in rats at oral doses as low as one tenth the 40 mg clinical daily dose (see Data).

Bisphosphonates are incorporated into the bone matrix, from which they are gradually released over a period of years. The amount of bisphosphonate incorporated into adult bone~~,~~ and ~~hence, the amount~~ available for release ~~back~~ into the systemic circulation~~,~~ is directly related to the dose and duration of bisphosphonate use. ~~There are no data~~ Consequently, based on ~~fetal risk in humans. However,~~ the mechanism of action of bisphosphonates, there is a ~~theoretical~~ potential risk of fetal harm, predominantly skeletal, if a woman becomes pregnant after completing a course of bisphosphonate therapy. The impact of variables such as time between

cessation of bisphosphonate therapy to conception, the particular bisphosphonate used, and the route of administration (intravenous versus oral) on the risk has not been studied.

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

Data

Animal Data

Reproduction studies in rats dosed orally from before mating to the end of gestation or lactation showed decreased postimplantation survival starting at 2 mg/kg/day and decreased body weight gain ~~in normal pups~~ starting at 1 mg/kg/day, doses equivalent to less than half ~~of~~ the ~~recommended~~ 40 mg clinical ~~dose.~~ daily dose based on body surface area, mg/m2. Incidence of incomplete fetal ossification in vertebral, skull, and sternebral bones were ~~statistically significantly~~ increased in rats ~~beginning at~~ dosed orally during organogenesis starting at 10 mg/kg/day (approximately 3 times the 40 mg clinical daily dose ~~in vertebral (cervical, thoracic, and lumber), skull, and sternebral bones~~). No similar fetal effects were ~~seen when~~ observed in pregnant rabbits ~~were treated with doses~~ dosed orally during organogenesis at up to 35 mg/kg/day (equivalent to approximately 10 times the 40 mg clinical daily dose).

Both total and ionized calcium decreased in pregnant rats ~~at~~ dosed orally with 15 mg/kg/day alendronate (approximately 4 times the 40 mg clinical daily dose) resulting in delays and failures of delivery. Protracted parturition due to maternal hypocalcemia ~~occurred in rats at doses as low as one tenth the clinical dose~~ was observed when rats were treated from before mating through gestation~~.~~ starting at 0.5 mg/kg/day (approximately one tenth the 40 mg clinical daily dose). Maternotoxicity (late pregnancy deaths) also occurred in ~~the~~ female rats treated ~~at~~ orally with 15 mg/kg/day (approximately 4 times the 40 mg clinical daily dose) for varying gestational time periods. ~~Of time ranging from treatment only during pre-mating to treatment only during early, middle, or late gestational time; these~~ These maternal deaths were lessened but not eliminated by cessation of treatment. Calcium supplementation ~~either~~ in the drinking water or by subcutaneous minipump to rats dosed orally with 15 mg/kg/day alendronate could not ameliorate the hypocalcemia or prevent the dystocia-related maternal and neonatal deaths. ~~Due to delays in delivery;~~ However, intravenous calcium supplementation prevented maternal, but not ~~fetal~~ neonatal deaths.

~~Exposure multiples based on surface area, mg/m^2, were calculated using a 40 mg human daily dose. Animal dose ranged between 1 and 15 mg/kg/day in rats and up to 40 mg/kg/day in rabbits~~

8.2 Lactation ~~Nursing Mothers~~

Risk Summary

It is not known whether alendronate is ~~excreted~~ present in human breast milk~~. Because many drugs are excreted in~~, affects human milk~~, caution~~ production, or has effects on the breastfed infant. The developmental and health benefits of breastfeeding should be ~~exercised when~~ considered along with the mother's clinical need for FOSALAN ~~is administered to nursing~~ women and any potential adverse effects on the breastfed child from FOSALAN or from the underlying maternal condition.

<u>עדכונים מהותיים בעלון לצרכן:</u>

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2.2 אזהרות מיוחדות בנוגע לשימוש בפוסאלאן
לפני התחלת הטיפול בפוסאלאן, ספר לרופא שלך אם:

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- יש לך סרטן
- הינך בהריון, ~~או מתכננת הריון~~ <u>מנסה להרות או חושדת שהינך בהריון</u>. **<u>אם נכנסת להריון בזמן נטילת פוסאלאן, הפסיקי ליטול אותה וצרי קשר עם הרופא שלך.</u>** לא ידוע האם **פוסאלאן** יכולה להזיק לעובר שלך

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2.5 הריון והנקה

לפני התחלת הטיפול ב**פוסאלאן**, ספרי לרופא שלך אם:

- הינך בהריון ~~או מתכננת הריון~~, <u>מנסה להרות או חושדת שהינך בהריון</u>. **<u>אם נכנסת להריון בזמן נטילת פוסאלאן, הפסיקי ליטול אותה וצרי קשר עם הרופא שלך.</u>** לא ידוע האם **פוסאלאן** יכולה להזיק לעובר שלך

בעלונים לרופא ולצרכן היו עדכונים נוספים שאינם מהותיים ואינם נכללים בהודעה זו.
העלון לרופא והעלון לצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום, חברת MSD, בטלפון 09-9533333.
Fosalan OW 70mg מופצת ע"י חברת נובולוג בע"מ.

בברכה,
דורית מאורי
רוקחת ממונה
MSD ישראל

References:
Fosalan_OW_tabs-PC-08_2020
Fosalan_WO_tabs-PPI_HEB-08_2020