



יולי 2019

רופא/ה, רוקח/ת נכבד/ה,

Azenil Capsules

ברצוננו להודיעך על עדכון בעלון לרופא ובעלון לצרכן של התכשירים הבאים:

Azenil 200mg/5ml Suspension

המרכיב הפעיל:

Azenil Capsules: Azithromycin (as dihydrate) 250mg

Azenil 200mg/5ml suspension : Azithromycin (as dihydrate) 200mg/5ml

Indicated for:

Infections caused by susceptible organisms in lower respiratory tract including bronchitis and pneumonia, skin and soft tissue infections, otitis media, upper respiratory tract infections including sinusitis and pharyngitis, tonsillitis, also in the treatment of uncomplicated genital infections due to chlamydia trachomatis.

להלן העדכונים העיקריים בעלון לרופא:

6 DRUG INTERACTIONS

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6.3 Potential Drug-Drug Interactions Interaction with Macrolides

Interactions with digoxin, or colchicine or phenytoin have not been reported in clinical trials with azithromycin. ~~however, no.~~ No specific drug interaction studies have been performed to evaluate potential drug-drug ~~interactions~~ interaction. However, drug interactions have been observed with other macrolide products. Until further data are developed regarding drug interactions when digoxin, colchicine - or phenytoin are used ~~concomitantly~~ with azithromycin careful monitoring of patients is advised.

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7 USE IN SPECIFIC POPULATIONS

7.1 Pregnancy

~~Teratogenic Effects: Pregnancy Category B: Reproduction studies have been performed in rats and mice at doses up to moderately maternally toxic dose concentrations (i.e., 200 mg/kg/day). These daily doses in rats and mice, based on body surface area, are estimated to be 4 and 2 times, respectively, an adult daily dose of 500 mg. In the animal studies, no evidence of harm to the fetus due to azithromycin was found. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, azithromycin should be used during pregnancy only if clearly needed.~~

~~**7.2 Nursing Mothers**~~

~~Azithromycin has been reported to be excreted in human breast milk in small amounts. Caution should be exercised when azithromycin is administered to a nursing woman.~~

Risk Summary

Available data from published literature and postmarketing experience over several decades with azithromycin use in pregnant women have not identified any drug-associated risks for major birth defects, miscarriage, or adverse maternal or fetal outcomes (see Data). Developmental toxicity studies with azithromycin in rats, mice, and rabbits showed no drug-induced fetal malformations at doses up to 4, 2, and 2 times, respectively, an adult human daily dose of 500 mg based on body surface area. Decreased viability and delayed development were observed in the offspring of pregnant rats

administered azithromycin from day 6 of pregnancy through weaning at a dose equivalent to 4 times an adult human daily dose of 500 mg based on body surface area (see Data).

The estimated background risk of major birth defects and miscarriage for the indicated populations 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.

Data

Human Data

Available data from published observational studies, case series, and case reports over several decades do not suggest an increased risk for major birth defects, miscarriage, or adverse maternal or fetal outcomes with azithromycin use in pregnant women. Limitations of these data include the lack of randomization and inability to control for confounders such as underlying maternal disease and maternal use of concomitant medications.

Animal Data

Azithromycin administered during the period of organogenesis did not cause fetal malformations in rats and mice at oral doses up to 200 mg/kg/day (moderately maternally toxic). Based on body surface area, this dose is approximately 4 (rats) and 2 (mice) times an adult human daily dose of 500 mg. In rabbits administered azithromycin at oral doses of 10, 20, and 40 mg/kg/day during organogenesis, reduced maternal body weight and food consumption were observed in all groups; no evidence of fetotoxicity or teratogenicity was observed at these doses, the highest of which is estimated to be 2 times an adult human daily dose of 500 mg based on body surface area.

In a pre- and postnatal development study, azithromycin was administered orally to pregnant rats from day 6 of pregnancy until weaning at doses of 50 or 200 mg/kg/day. Maternal toxicity (reduced food consumption and body weight gain; increased stress at parturition) was observed at the higher dose. Effects in the offspring were noted at 200 mg/kg/day during the postnatal development period (decreased viability, delayed developmental landmarks). These effects were not observed in a pre- and postnatal rat study when up to 200 mg/kg/day of azithromycin was given orally beginning on day 15 of pregnancy until weaning.

7.2 Lactation

Risk Summary

Azithromycin is present in human milk (see Data). Non-serious adverse reactions have been reported in breastfed infants after maternal administration of azithromycin (see Clinical Considerations). There are no available data on the effects of azithromycin on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for AZENIL and any potential adverse effects on the breastfed infant from AZENIL or from the underlying maternal condition.

Clinical Considerations

Advise women to monitor the breastfed infant for diarrhea, vomiting, or rash.

Data

Azithromycin breastmilk concentrations were measured in 20 women after receiving a single 2 g oral dose of azithromycin during labor. Breastmilk samples collected on days 3 and 6 postpartum as well as 2 and 4 weeks postpartum revealed the presence of azithromycin in breastmilk up to 4 weeks after dosing. In another study, a single dose of azithromycin 500 mg was administered intravenously to 8 women prior to incision for cesarean section. Breastmilk (colostrum) samples obtained between 12 and 48 hours after dosing revealed that azithromycin persisted in breastmilk up to 48 hours.

להלן העדכונים העיקריים בעלון לצרכן :

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2. לפני השימוש בתרופה

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- אם אתה לוקח, או לקחת לאחרונה, תרופות אחרות כולל תרופות ללא מרשם ותוספי תזונה, ספר על כך לרופא או לרוקח. במיוחד יש ליידע את הרופא או הרוקח אם אתה לוקח:**
- גלפינאביר (לטיפול באיידס) מכיוון שהשילוב עלול להעלות את רמות האזיתרומיצין בדם.

• תכשירים נוגדי קרישה (כגון [אדפריין](#) ו**אארפרין**) – יש להיות במעקב אחרי מדדי קרישה.

• [פניטואין](#)

• דיגוקסין.

• [קולכיצין](#).

• [פניטואין](#).

• תכשירים נוגדי חומצה המכילים אלומיניום או מגנזיום.

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השינויים המודגשים ברקע צהוב מהווים החמרה. כמו כן, בוצעו שינויים נוספים הכוללים תוספת מידע, השמטת מידע ועדכוני נוסח שאינם מהווים החמרה. בהודעה זו מצוינים רק העדכונים העיקריים. קיימים עדכונים נוספים.

העלונים המעודכנים נשלחו למשרד הבריאות לצורך פרסומם במאגר התרופות שבאתר משרד הבריאות:
<https://www.old.health.gov.il/units/pharmacy/trufot/index.asp?safa=h>

לחילופין, לקבלת עלונים מלאים מודפסים ניתן לפנות לחברת פיזר פי אף אי פרמצבטיקה ישראל בע"מ
שנקר 9, ת.ד. 12133
הרצליה פיתוח, 46725.

בברכה,
עשת אושרית
רוקחת ממונה