פייזר פי אף אי פרמצבטיקה ישראל בע"מ
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פברואר 2020

רופא/ה, רוקח/ת נכבד/ה,

חב' פייזר פי אף אי מבקשת להודיע על עדכון בעלונים לרופא ולצרכן של התכשיר **TYGACIL**

המרכיב הפעיל בתכשיר:

TIGECYCLINE 50 mg

התוויה רשומה:

Indicated for:
TYGACIL is indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the conditions listed below for patients 18 years of age and older:
Complicated Skin and Skin Structure Infections:
Complicated skin and skin structure infections caused by Escherichia coli, Enterococcus faecalis (vancomycinsusceptible isolates), Staphylococcus aureus (methicillin-susceptible and -resistant isolates), Streptococcus agalactiae, Streptococcus anginosus grp. (includes S. anginosus, S. intermedius, and S. constellatus), Streptococcus pyogenes, Enterobacter cloacae, Klebsiella pneumoniae, and Bacteroides fragilis
Complicated Intra-abdominal Infections:
Complicated intra-abdominal infections caused by Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Enterococcus faecalis (vancomycin-susceptible isolates), Staphylococcus aureus (methicillin-susceptible and -resistant isolates), Streptococcus anginosus grp. (includes S. anginosus, S. intermedius, and S. constellatus), Bacteroides fragilis, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Clostridium perfringens, and Peptostreptococcus micros.
Community-Acquired Bacterial Pneumonia:
Community-acquired bacterial pneumonia caused by Streptococcus pneumoniae (penicillin susceptible isolates), including cases with concurrent bacteremia, Haemophilus influenzae (beta-lactamase negative isolates), and Legionella pneumophila.

להלן העדכונים העיקריים בעלון לרופא:

5. Special warnings and precautions for use
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5.6 Tooth Discoloration and Enamel Hypoplasia

The use of TYGACIL during tooth development (last half of pregnancy, infancy, and childhood to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown). This adverse reaction is more common during long-term use of tetracyclines, but it has been observed following repeated short-term courses. Enamel hypoplasia has also been reported. Advise the patient of the potential risk to the fetus if TYGACIL is used during the second or third trimester of pregnancy

5.7 Inhibition of Bone Growth

The use of TYGACIL during the second and third trimester of pregnancy, infancy and childhood up to the age of 8 years may cause reversible inhibition of bone growth. All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate has been observed in premature infants given oral tetracycline in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the tetracycline was discontinued. Advise the patient of the potential risk to the fetus if TYGACIL is used during the second or third trimester of pregnancy.

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8. USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary

TYGACIL, like other tetracycline class antibacterial drugs, may cause permanent discoloration of deciduous teeth and reversible inhibition of bone growth when administered during the second and

third trimesters of pregnancy. There are no available data on the risk of major birth defects or miscarriage following the use of TYGACIL during pregnancy. Administration of intravenous tigecycline in pregnant rats and rabbits during the period of organogenesis was associated with reduction in fetal weights and an increased incidence of skeletal anomalies (delays in bone ossification) at exposures of 5 and 1 times the human exposure at the recommended clinical dose in rats and rabbits, respectively. Advise the patient of the potential risk to the fetus if TYGACIL is used during the second or third trimester.

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 in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Human Data

The use of tetracycline-class antibacterial drugs, that includes TYGACIL, during tooth development (second and third trimester of pregnancy) may cause permanent discoloration of deciduous teeth. This adverse reaction is more common during long-term use of tetracyclines but has been observed following repeated short-term courses. TYGACIL may cause reversible inhibition of bone growth when administered during the second and third trimesters of pregnancy. A decrease in fibula growth rate has been observed in premature infants given oral tetracycline in doses of 25 mg/kg every 6 hours.

Animal Data

In embryo-fetal development studies, tigecycline was administered during the period of organogenesis at doses up to 12 mg/kg/day in rats and 4 mg/kg in rabbits or 5 and 1 times the systemic exposure at the recommended clinical dose, respectively. In the rat study, decreased fetal weight and fetal skeletal variations (reduced ossification of the pubic, ischial, and supraoccipital bones and increased incidences of rudimentary 14^{th} rib) were observed in the presence of maternal toxicity at 12 mg/kg/day (5 times the recommended clinical dose based on systemic exposure). In rabbits, decreased fetal weights were observed in the presence of maternal toxicity at 4 mg/kg (equivalent to the human exposure at the recommended clinical dose).

In preclinical safety studies, ^{14}C-labeled tigecycline crossed the placenta and was found in fetal tissues.

8.2 Lactation

Risk Summary

There are no data on the presence of tigecycline in human milk; however, tetracycline-class antibacterial drugs are present in breast milk. It is not known whether tigecycline has an effect on the breastfed infant or on milk production. Tigecycline has low oral bioavailability; therefore, infant exposure is expected to be low. Tigecycline is present in rat milk with little or no systemic exposure to tigecycline in nursing pups as a result of exposure via maternal milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk.

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

Clinical Considerations

Because of the theoretical risk of dental discoloration and inhibition of bone growth, avoid breastfeeding if taking TYGACIL for longer than three weeks. A lactating woman may also consider interrupting breastfeeding and pumping and discarding breastmilk during administration of TYGACIL and for 9 days (approximately 5 half-lives) after the last dose in order to minimize drug exposure to a breastfed

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השינויים המודגשים בצהוב מהווים החמרה. כמו כן, בוצעו שינויים נוספים הכוללים תוספת מידע, השמטת מידע ועדכוני נוסח שאינם מהווים החמרה.

העלונים המעודכים נשלחו למשרד הבריאות לצורך פרסומם במאגר התרופות שבאתר משרד הבריאות:
https://data.health.gov.il/drugs/index.html#!/byDrug

לחילופין, לקבלת עלונים מלאים מודפסים ניתן לפנות לחברת פייזר פי אף אי פרמצבטיקה ישראל בע"מ
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בברכה,
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