מרץ 2019

שם התכשיר:

Amaryl 1mg tablets
Amaryl 2mg tablets
Amaryl 3mg tablets
Amaryl 4mg tablets

חומר פעיל: כל טבליה מכילה בהתאמה: Glimepiride 1mg, 2mg, 3mg, 4mg .

ההתוויה המאושרת הינה:

Amaryl is indicated for non-insulin-dependent diabetes melitus (adult-onset diabetes, type II diabetes), when diet, regular physical exercise and weight reduction alone cannot maintain therapeutically suitable blood glucose levels.

חברת סאנופי אוונטיס ישראל בע"מ מבקשת להודיע על עדכון העלון לרופא והעלון לצרכן בפברואר 2019.

מפורטים להלן רק תתי הסעיפים בהם נעשו העדכונים העיקריים בעלונים.

בעלון לרופא:

CONTRAINDICATIONS

AMARYL is contraindicated in patients with a history of a hypersensitivity reaction to:

- Glimepiride or any of the product's ingredients *[see Warnings and Precautions (5.2]*.

- Sulfonamide derivatives: Patients who have developed an allergic reaction to sulfonamide derivatives may develop an allergic reaction to AMARYL. Do not use AMARYL in patients who have a history of an allergic reaction to sulfonamide derivatives.

~~Reported hypersensitivity reactions include cutaneous eruptions with or without pruritus as well as more serious reactions (e.g. anaphylaxis, angioedema, Stevens-Johnson Syndrome, dyspnea) [see *Warnings and Precautions (5.2) and Adverse Reactions (6.2)*].~~

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9.1 Pregnancy

~~**Pregnancy Category C**~~
~~There are no adequate and well-controlled studies of AMARYL in pregnant women. In animal studies there was no increase in congenital anomalies, but an increase in fetal deaths occurred in rats and rabbits at glimepiride doses 50 times (rats) and 0.1 times (rabbits) the maximum recommended human dose (based on body surface area). This fetotoxicity, observed only at doses inducing maternal hypoglycemia, is believed to be directly related to the pharmacologic (hypoglycemic) action of glimepiride and has been similarly noted with other sulfonylureas. AMARYL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Because data suggest that abnormal blood glucose during pregnancy is associated with a higher incidence of congenital abnormalities, diabetes treatment during pregnancy should maintain blood glucose as close to normal as possible.~~

~~*Nonteratogenic Effects:* Prolonged severe hypoglycemia (4 to 10 days) has been reported in neonates born to mothers receiving a sulfonylurea at the time of delivery.~~

Risk Summary

Available data from a small number of published studies and postmarketing experience with AMARYL use in pregnancy over decades have not identified any drug associated risks for major birth defects, miscarriage, or adverse maternal outcomes. However, sulfonylureas (including glimepiride) cross the placenta and have been associated with neonatal adverse reactions such as hypoglycemia. Therefore, AMARYL should be discontinued at least two weeks before expected delivery *(see Clinical Considerations)*. Poorly controlled diabetes in pregnancy is also associated with risks to the mother and fetus *(see Clinical Considerations)*. In animal studies *(see Data)*, there were no effects on embryo-fetal development following administration of glimepiride to pregnant rats and rabbits at oral doses approximately 4000 times and 60 times the maximum human dose based on body surface area, respectively. However, fetotoxicity was observed in rats and rabbits at doses 50 times and 0.1 times the maximum human dose, respectively.

The estimated background risk of major birth defects is 6% to 10% in women with pre-gestational diabetes with a HbA1c >7% and has been reported to be as high as 20% to 25% in women with a HbA1c >10%. The estimated background risk of miscarriage for the indicated population is unknown. 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

Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoacidosis, preeclampsia, spontaneous abortions, preterm delivery, and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, still birth, and macrosomia-related morbidity.

Fetal/neonatal adverse reactions

Neonates of women with gestational diabetes who are treated with sulfonylureas during pregnancy may be at increased risk for neonatal intensive care admission and may develop respiratory distress, hypoglycemia, birth injury, and be large for gestational age. Prolonged severe hypoglycemia, lasting 4–10 days, has been reported in neonates born to mothers receiving a sulfonylurea at the time of delivery and has been reported with the use of agents with a prolonged half-life. Observe newborns for symptoms of hypoglycemia and respiratory distress and manage accordingly.

Dose adjustments during pregnancy and the postpartum period

Due to reports of prolonged severe hypoglycemia in neonates born to mothers receiving a sulfonylurea at the time of delivery, AMARYL should be discontinued at least two weeks before expected delivery *(see Fetal/Neonatal Adverse Reactions).*

Data

Animal data

In animal studies, there was no increase in congenital anomalies, but an increase in fetal deaths occurred in rats and rabbits at glimepiride doses 50 times (rats) and 0.1 times (rabbits) the maximum recommended human dose (based on body surface area). This fetotoxicity was observed only at doses inducing maternal hypoglycemia and is believed to be directly related to the pharmacologic (hypoglycemic) action of glimepiride, as has been similarly noted with other sulfonylureas.

9.2 Lactation~~Nursing Mothers~~

~~It is not known whether AMARYL is excreted in human milk. During pre- and post-natal studies in rats, significant concentrations of glimepiride were present in breast milk and the serum of the pups. Offspring of rats exposed to high levels of glimepiride during pregnancy and lactation developed skeletal deformities consisting of shortening, thickening, and bending of the humerus during the postnatal period. These skeletal deformations were determined to be the result of nursing from mothers exposed to glimepiride. Based on these animal data and the potential for hypoglycemia in a nursing infant, a decision should be made whether to discontinue nursing or discontinue AMARYL, taking into account the importance of AMARYL to the mother.~~

Risk Summary

Breastfed infants of lactating women using AMARYL should be monitored for symptoms of hypoglycemia *(see Clinical Considerations).* It is not known whether glimepiride is excreted in human milk and there are no data on the effects of glimepiride on milk production. Glimepiride is present in rat milk *[see Data]*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for AMARYL and any potential adverse effects on the breastfed child from AMARYL or from the underlying maternal condition.

Clinical Considerations

Monitoring for adverse reactions

Monitor breastfed infants for signs of hypoglycemia (e.g., jitters, cyanosis, apnea, hypothermia, excessive sleepiness, poor feeding, seizures).

Data

During prenatal and postnatal studies in rats, significant concentrations of glimepiride were present in breast milk and the serum of the pups. Offspring of rats exposed to high levels of glimepiride during pregnancy and lactation developed skeletal deformities consisting of shortening, thickening, and bending of the humerus during the postnatal period. These skeletal deformations were determined to be the result of nursing from mothers exposed to glimepiride.

בעלון לצרכן, עודכן הסעיף הבא:

הריון, הנקה ופוריות:

אם הנך בהריון, מתכננת הריון, מניקה או מתכננת להניק יש להיוועץ ברופא לפני השימוש בתרופות.

אם הנך מניקה, יש לעקוב אחר סימנים של היפוגליקמיה אצל התינוק (לדוגמא, עצבנות, כיחלון, הפסקת נשימה, חום נמוך, שינה מוגברת, אי רצון לאכול, פרכוסים).

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים על ידי פנייה לבעל הרישום- סאנופי-אוונטיס ישראל בע"מ, רח' בני גאון 10 נתניה או בטלפון: 09-8633700.

להלן הקישור לאתר משרד הבריאות:

https://data.health.gov.il/drugs/index.html#/byDrug

בברכה,

גליה הוכשטד

רוקחת ממונה

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