אפריל 2022

רופא /ה, רוקח/ת נכבד/ה

חברת טבע מודיעה על העדכונים הבאים בעלונים לצרכן ולרופא של התכשיר

קלונקס 0.5 מ״ג/קלונקס 2 מ״ג, טבליות

CLONEX 0.5 mg \CLONEX 2 mg, Tablets

Contains: ***0.5 mg Clonazepam\ 2 mg Clonazepam***

עדכונים בעלון לרופא ובעלון לצרכן

התוויה כפי שאושרה בתעודת הרישום:

- Typical or atypical petit mal,Lennox - Gastaut syndrome (petit mal variant), generalized primary or secondary tonic-clonic seizures including grand mal and focal seizures.
- Panic disorder

ברצוננו להודיע שהעלונים לרופא ולצרכן עודכנו, בפירוט שלהלן כלולים העדכונים העיקריים בלבד (תוספות מסומנות באדום והסרות מידע כטקסט מחוק):

שינויים בעלון לרופא:

7. WARNINGS

[…]

Neonatal Sedation and Withdrawal Syndrome:

Use of clonazepam late in pregnancy can result in sedation (respiratory depression, lethargy, hypotonia) and/or withdrawal symptoms (hyperreflexia, irritability, restlessness, tremors, inconsolable crying, and feeding difficulties) in the neonate (see PRECAUTIONS: Pregnancy). Monitor neonates exposed to clonazepam during pregnancy or labor for signs of sedation and monitor neonates exposed to clonazepam during pregnancy for signs of withdrawal; manage these neonates accordingly

8. PRECAUTIONS

Pregnancy

~~Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy with clonazepam~~ Advise pregnant females that use of clonazepam late in pregnancy can result in sedation (respiratory depression, lethargy, hypotonia) and/or withdrawal symptoms (hyperreflexia, irritability, restlessness, tremors, inconsolable crying, and feeding difficulties) in newborns.
Instruct patients to inform their healthcare provider if they are pregnant

Nursing

[…] Instruct breastfeeding patients who take clonazepam to monitor their infants for excessive sedation, poor feeding and poor weight gain, and to seek medical attention if they notice these signs

10. PREGNANCY

Risk Summary

Neonates born to mothers using benzodiazepines late in pregnancy have been reported to experience symptoms of sedation and/or neonatal withdrawal. Available data from published observational studies of pregnant women exposed to benzodiazepines do not report a clear association with benzodiazepines and major birth defects (see Data).
Administration of clonazepam to pregnant rabbits during the period of organogenesis resulted in developmental toxicity, including increased incidences of fetal malformations, at doses similar to or below therapeutic doses in patients (see Animal Data). Data for other benzodiazepines suggest the possibility of long-term effects on neurobehavioral and immunological function in animals following prenatal exposure to benzodiazepines at clinically relevant doses.
The 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 risk of major birth defects and of miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations Fetal/Neonatal Adverse Reactions

Benzodiazepines cross the placenta and may produce respiratory depression, hypotonia and sedation in neonates. Monitor neonates exposed to clonazepam during pregnancy or labor for signs of sedation, respiratory depression, hypotonia, and feeding problems. Monitor neonates exposed to clonazepam during pregnancy for signs of withdrawal.
Manage these neonates accordingly

Data Human Data

Published data from observational studies on the use of benzodiazepines during pregnancy do not report a clear association with benzodiazepines and major birth defects.
Although early studies reported an increased risk of congenital malformations with diazepam and chlordiazepoxide, there was no consistent pattern noted. In addition, the majority of more recent case-control and cohort studies of benzodiazepine use during pregnancy, which were adjusted for confounding exposures to alcohol, tobacco and other medications, have not confirmed these findings.

12. NURSING MOTHERS

Risk summary

Clonazepam is excreted in human milk. There are reports of sedation, poor feeding and poor weight gain in infants exposed to benzodiazepines through breast milk. There are no data on the effects of clonazepam on milk production
[...]

Clinical Considerations

Infants exposed to clonazepam through breast milk should be monitored for sedation, poor feeding and poor weight gain

18. OVERDOSE

Overdosage of benzodiazepines is characterized by central nervous system depression ranging from drowsiness to coma. In mild to moderate cases, symptoms can include drowsiness, confusion, dysarthria, lethargy, hypnotic state, diminished reflexes, ataxia, and hypotonia. Rarely, paradoxical or disinhibitory reactions (including agitation, irritability, impulsivity, violent behavior, confusion, restlessness, excitement, and talkativeness) may occur. In severe overdosage cases, patients may develop respiratory depression and coma. Overdosage of benzodiazepines in combination with other CNS depressants (including alcohol and opioids) may be fatal. Markedly abnormal (lowered or elevated) blood pressure, heart rate, or respiratory rate raise the concern that additional drugs and/or alcohol are involved in the overdosage. [...] ~~Hypotension may be combated by the use of levarterenol or metaraminol. Dialysis is of no known value.~~

[...] in the management of benzodiazepine overdosage, can lead to withdrawal and adverse reactions, including seizures, particularly in the context of mixed overdosage with drugs that increase seizure risk (e.g., tricyclic and tetracyclic antidepressants) and in patients with long-term benzodiazepine use and physical dependency. The risk of withdrawal seizures with flumazenil use may be increased in patients with epilepsy. Flumazenil is contraindicated in patients who have received a benzodiazepine for control of a potentially life-threatening condition (e.g., status epilepticus).

If the decision is made to use flumazenil, it should be used as an adjunct to, not as a substitute for, supportive management of benzodiazepine overdosage

~~Patients treated with flumazenil should be monitored for resedation, respiratory depression and other residual benzodiazepine effects for an appropriate period after treatment. The prescriber should be aware of a risk of seizure in association with flumazenil treatment, particularly in long-term benzodiazepine users and in cyclic antidepressant overdose. The complete flumazenil package insert, including CONTRAINDICATIONS, WARNINGS and PRECAUTIONS, should be consulted prior to use Flumazenil is not indicated in patients with epilepsy who have been treated with benzodiazepines. Antagonism of the benzodiazepine effect in such patients may provoke seizures~~

~~Serious sequelae are rare unless other drugs or alcohol have been taken concomitantly.~~

<u>שינויים בעלון לצרכן:</u>

<u>2. לפני השימוש בתרופה</u>

[...]

היריון והנקה

היריון

- ~~מחקרים שנעשו על בעלי חיים הראו השפעות מזיקות של תרופות מקבוצת הבנזודיאזפינים (כולל תרופות המכילות קלונזפאם, המרכיב הפעיל בקלונקס) על העובר המתפתח.~~
- ילדים שנולדו לאימהות אשר קיבלו בשלבי ההיריון המתקדמים תרופות מקבוצת הבנזודיאזפינים (כולל תרופות עם קלונזפאם), עלולים להיות בסיכון לסימפטומים של סדציה (בעיות נשימה, לבעיות אכילה, ~~לתת-חום (היפותרמיה)~~ עצלות/כבדות טונוס/מתח שרירים נמוך) ו/או ולתסמיני גמילה

העלון לצרכן נשלח לפרסום במאגר התרופות שבאתר האינטרנט של משרד הבריאות

https://israeldrugs.health.gov.il, וניתן לקבלו מודפס ע"י פניה לחברת טבע.