



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:**

**WARNING: RISKS FROM CONCOMITANT USE WITH OPIOIDS; ABUSE, MISUSE, AND ADDICTION; and DEPENDENCE AND WITHDRAWAL REACTIONS**

[...]

- The use of benzodiazepines, including clonazepam tablets, exposes users to risks of abuse, misuse, and addiction, which can lead to overdose or death. Abuse and misuse of benzodiazepines commonly involve concomitant use of other medications, alcohol, and/or illicit substances, which is associated with an increased frequency of serious adverse outcomes. Before prescribing clonazepam tablets and throughout treatment, assess each patient's risk for abuse, misuse, and addiction (see WARNINGS).
- The continued use of benzodiazepines, including clonazepam tablets, may lead to clinically significant physical dependence. The risks of dependence and withdrawal increase with longer treatment duration and higher daily dose. Abrupt discontinuation or rapid dosage reduction of clonazepam tablets after continued use may precipitate acute withdrawal reactions, which can be life-threatening. To reduce the risk of withdrawal reactions, use a gradual taper to discontinue clonazepam tablets or reduce the dosage (see DOSAGE AND ADMINISTRATION and WARNINGS).



## 7. WARNINGS

[...]

### **Abuse, Misuse, and Addiction**

The use of benzodiazepines, including clonazepam tablets, exposes users to the risks of abuse, misuse, and addiction, which can lead to overdose or death. Abuse and misuse of benzodiazepines often (but not always) involve the use of doses greater than the maximum recommended dosage and commonly involve concomitant use of other medications, alcohol, and/or illicit substances, which is associated with an increased frequency of serious adverse outcomes, including respiratory depression, overdose, or death (see **DRUG ABUSE AND DEPENDENCE: Abuse**).

Before prescribing clonazepam tablets and throughout treatment, assess each patient's risk for abuse, misuse, and addiction (e.g., using a standardized screening tool). Use of clonazepam tablets, particularly in patients at elevated risk, necessitates counseling about the risks and proper use of clonazepam tablets along with monitoring for signs and symptoms of abuse, misuse, and addiction. Prescribe the lowest effective dosage; avoid or minimize concomitant use of CNS depressants and other substances associated with abuse, misuse, and addiction (e.g., opioid analgesics, stimulants); and advise patients on the proper disposal of unused drug. If a substance use disorder is suspected, evaluate the patient and institute (or refer them for) early treatment, as appropriate.

### **Dependence and Withdrawal Reactions**

To reduce the risk of withdrawal reactions, use a gradual taper to discontinue clonazepam tablets or reduce the dosage (a patient-specific plan should be used to taper the dose) (see **DOSAGE AND ADMINISTRATION: Discontinuation or Dosage Reduction of clonazepam tablets**).

Patients at an increased risk of withdrawal adverse reactions after benzodiazepine discontinuation or rapid dosage reduction include those who take higher dosages, and those who have had longer durations of use.

### **Acute Withdrawal Reactions**

The continued use of benzodiazepines, including clonazepam tablets, may lead to clinically significant physical dependence. Abrupt discontinuation or rapid dosage reduction of clonazepam tablets after continued use, or administration of flumazenil (a benzodiazepine antagonist) may precipitate acute withdrawal reactions, which can be life-threatening (e.g., seizures) (see **DRUG ABUSE AND DEPENDENCE: Dependence**).

### **Protracted Withdrawal Syndrome**

In some cases, benzodiazepine users have developed a protracted withdrawal syndrome with withdrawal symptoms lasting weeks to more than 12 months (see **DRUG ABUSE AND DEPENDENCE: Dependence**).

[...]



## 8. PRECAUTIONS

[...]

### Risks from Concomitant Use with Opioids

#### *Abuse, Misuse, and Addiction*

Inform patients that the use of clonazepam tablets, even at recommended dosages, exposes users to risks of abuse, misuse, and addiction, which can lead to overdose and death, especially when used in combination with other medications (e.g., opioid analgesics), alcohol, and/or illicit substances. Inform patients about the signs and symptoms of benzodiazepine abuse, misuse, and addiction; to seek medical help if they develop these signs and/or symptoms; and on the proper disposal of unused drug (see **WARNINGS: Abuse, Misuse, and Addiction** and **DRUG ABUSE AND DEPENDENCE**).

#### *Withdrawal Reactions*

Inform patients that the continued use of clonazepam tablets may lead to clinically significant physical dependence and that abrupt discontinuation or rapid dosage reduction of clonazepam tablets may precipitate acute withdrawal reactions, which can be life-threatening. Inform patients that in some cases, patients taking benzodiazepines have developed a protracted withdrawal syndrome with withdrawal symptoms lasting weeks to more than 12 months. Instruct patients that discontinuation or dosage reduction of clonazepam tablets may require a slow taper (see **WARNINGS: Dependence and Withdrawal Reactions** and **DRUG ABUSE AND DEPENDENCE**).

[...]

## 17. DRUG ABUSE AND DEPENDENCE

[...]

### **17.2 Abuse:**

Clonazepam tablets is a benzodiazepine and a CNS depressant with a potential for abuse and addiction. Abuse is the intentional, non-therapeutic use of a drug, even once, for its desirable psychological or physiological effects. Misuse is the intentional use, for therapeutic purposes, of a drug by an individual in a way other than prescribed by a health care provider or for whom it was not prescribed. Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use (e.g., continuing drug use despite harmful consequences, giving a higher priority to drug use than other activities and obligations), and possible tolerance or physical dependence. Even taking benzodiazepines as prescribed may put patients at risk for abuse and misuse of their medication. Abuse and misuse of benzodiazepines may lead to addiction.

Abuse and misuse of benzodiazepines often (but not always) involve the use of doses greater than the maximum recommended dosage and commonly involve concomitant use of other medications, alcohol, and/or illicit substances, which is associated with an increased frequency of serious adverse outcomes, including respiratory depression, overdose, or death. Benzodiazepines are often sought by individuals who abuse drugs and other substances, and by individuals with addictive disorders (see **WARNINGS: Abuse, Misuse, and Addiction**).

The following adverse reactions have occurred with benzodiazepine abuse and/or misuse: abdominal pain, amnesia, anorexia, anxiety, aggression, ataxia, blurred vision, confusion, depression, disinhibition, disorientation, dizziness, euphoria, impaired



concentration and memory, indigestion, irritability, muscle pain, slurred speech, tremors, and vertigo.

The following severe adverse reactions have occurred with benzodiazepine abuse and/or misuse: delirium, paranoia, suicidal ideation and behavior, seizures, coma, breathing difficulty, and death. Death is more often associated with polysubstance use (especially benzodiazepines with other CNS depressants such as opioids and alcohol).

### ***17.3 Dependence***

#### ***Physical Dependence***

Clonazepam tablets may produce physical dependence from continued therapy. Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug. Abrupt discontinuation or rapid dosage reduction of benzodiazepines or administration of flumazenil, a benzodiazepine antagonist, may precipitate acute withdrawal reactions, including seizures, which can be life-threatening. Patients at an increased risk of withdrawal adverse reactions after benzodiazepine discontinuation or rapid dosage reduction include those who take higher dosages (i.e., higher and/or more frequent doses) and those who have had longer durations of use (see **WARNINGS: *Dependence and Withdrawal Reactions***).

To reduce the risk of withdrawal reactions, use a gradual taper to discontinue clonazepam tablets or reduce the dosage (see **DOSAGE AND ADMINISTRATION: *Discontinuation or Dosage Reduction of clonazepam tablets*** and **WARNINGS: *Dependence and Withdrawal Reactions***).

#### ***Acute Withdrawal Signs and Symptoms***

Acute withdrawal signs and symptoms associated with benzodiazepines have included abnormal involuntary movements, anxiety, blurred vision, depersonalization, depression, derealization, dizziness, fatigue, gastrointestinal adverse reactions (e.g., nausea, vomiting, diarrhea, weight loss, decreased appetite), headache, hyperacusis, hypertension, irritability, insomnia, memory impairment, muscle pain and stiffness, panic attacks, photophobia, restlessness, tachycardia, and tremor. More severe acute withdrawal signs and symptoms, including life-threatening reactions, have included catatonia, convulsions, delirium tremens, depression, hallucinations, mania, psychosis, seizures, and suicidality.

#### ***Protracted Withdrawal Syndrome***

Protracted withdrawal syndrome associated with benzodiazepines is characterized by anxiety, cognitive impairment, depression, insomnia, formication, motor symptoms (e.g., weakness, tremor, muscle twitches), paresthesia, and tinnitus that persists beyond 4 to 6 weeks after initial benzodiazepine withdrawal. Protracted withdrawal symptoms may last weeks to more than 12 months. As a result, there may be difficulty in differentiating withdrawal symptoms from potential re-emergence or continuation of symptoms for which the benzodiazepine was being used.

#### ***Tolerance***

Tolerance to clonazepam tablets may develop from continued therapy. Tolerance is a physiological state characterized by a reduced response to a drug after repeated administration (i.e., a higher dose of a drug is required to produce the same effect that was once obtained at a lower dose). Tolerance to the therapeutic effect of clonazepam tablets may develop; however, little tolerance develops to the amnestic reactions and other cognitive impairments caused by benzodiazepines.

[...]

## שינויים בעלון לצרכן:

### 2. לפני השימוש בתרופה

#### אזהרות מיוחדות הנוגעות לשימוש בתרופה

[...]

פנה לעזרה רפואית מיידית במקרים הבאים:

- נשימה שטחית ואיטית
- הפסקת נשימה (העלולה להוביל לדום לב)
- ישנוניות מופרזת (סדציה)

**קלונקס עלול לגרום לשימוש לרעה, שימוש מוטעה ותלות.** יש סיכון לשימוש לרעה, שימוש מוטעה ותלות בלקיחת תרופות ממשפחת בנזודיאזפינים, כולל קלונקס, אשר יכול להוביל למנת יתר ולתופעות לוואי חמורות הכוללות קומה ומוות.

- **תופעות לוואי חמורות כולל קומה ומוות קרו באנשים שהשתמשו בתרופה לרעה או בצורה לא נכונה.** תופעות לוואי חמורות אלו יכולות לכלול גם בלבול חריף, פרנויה, מחשבות או מעשים אובדניים, פרכוסים וקשיי נשימה. **במקרה של אחת מתופעות לוואי אלו יש לפנות מייד לרופא או לחדר מיון בבית החולים הקרוב.**
- **אתה יכול לפתח התמכרות גם אם אתה לקוח את התרופה כפי שרשם לך הרופא.**
- **יש לקחת בדיוק כפי שרשם לך הרופא.**
- אל תעביר את התרופה לאחרים
- שמור את התרופה במקום בטוח והרחק מילדים.

**תלות פיזית ותסמיני גמילה.** קלונקס עלול לגרום לתלות פיזית ותסמיני גמילה.

- **אין להפסיק לקיחה של קלונקס בצורה פתאומית.** הפסקה פתאומית של התרופה עלולה לגרום לתופעות לוואי חמורות ומסכנות חיים, כולל, תגובות, תנועות או הבעות בלתי רצוניות, פרכוסים, שינויים עיצביים או נפשיים חמורים ופתאומיים, דיכאון, שמיעה או ראייה של דברים שלא קיימים, עליה קיצונית בדיבור או פעילות, איבוד קשר עם המציאות, מחשבות או מעשים אובדניים. **במקרה של הופעת אחד מתסמינים אלו יש לפנות מייד לרופא או לחדר מיון בבית החולים הקרוב.**
- **אצל חלק מהאנשים שהפסיקו את התרופה באופן פתאומי היו תסמינים שנמשכו מספר שבועות עד ליותר מ- 12 חודשים, כולל, חרדה, קשיי זיכרון, למידה או ריכוז, דיכאון, קשיי שינה, תחושה מדומה של חרקים זוחלים מתחת לעור, חולשה, רעד, עוויתות שרירים, תחושה של צריבה או עקצוץ בידים, זרועות, רגליים או כפות רגליים, וצלצולים באוזניים.**
- תלות פיזית אינה זהה להתמכרות לתרופה. הרופא יוכל לספר לך על ההבדלים בין תלות פיזית בתרופה להתמכרות.
- אין לקחת מהתרופה מינון גבוה או לתקופה ארוכה יותר ממה שרשם לך הרופא.

[...]

העלון לצרכן נשלח לפרסום במאגר התרופות שבאתר האינטרנט של משרד הבריאות

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