CLONAZEPAM- clonazepam tablet
Northwind Pharmaceuticals

Patient Medication Guide

Clonazepam (klo-NAY-zeh-pam) Tablets USP, for oral use, CIV

What is the most important information I should know about clonazepam tablets?

Clonazepam tablets are a benzodiazepine medicine. Benzodiazepines can cause severe drowsiness, breathing problems (respiratory depression), coma, and death when taken with opioid medicines. Clonazepam tablets can make you sleepy or dizzy and can slow your thinking and motor skills. This may get better over time.

Do not drive, operate heavy machinery, or do other dangerous activities until you know how clonazepam tablets affect you.
Clonazepam tablets may cause problems with your coordination, especially when you are walking or picking things up.

Do not drink alcohol or take other drugs that may make you sleepy or dizzy while taking clonazepam tablets until you talk to your healthcare provider. When taken with alcohol or drugs that cause sleepiness or dizziness, clonazepam tablets may make your sleepiness or dizziness worse.
Like other antiepileptic drugs, clonazepam tablets may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.

Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:

thoughts about suicide or dying
attempt to commit suicide
new or worse depression
new or worse anxiety
feeling agitated or restless
panic attacks
trouble sleeping (insomnia)
new or worse irritability
acting aggressive, being angry, or violent
acting on dangerous impulses
an extreme increase in activity and talking (mania)
other unusual changes in behavior or mood

How can I watch for early symptoms of suicidal thoughts and actions?

Pay attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings. Keep all follow-up visits with your healthcare provider as scheduled.

Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

Suicidal thoughts or actions can be caused by things other than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other causes.

Do not stop clonazepam tablets without first talking to a healthcare provider.

Stopping clonazepam tablets suddenly can cause serious problems. Stopping clonazepam tablets suddenly can cause seizures that will not stop (status epilepticus).

Clonazepam tablets can cause abuse and dependence.

Do not stop taking clonazepam tablets all of a sudden. Stopping clonazepam tablets suddenly can cause

seizures that do not stop, hearing or seeing things that are not there (hallucinations), shaking, and stomach and muscle cramps.
Talk to your doctor about slowly stopping clonazepam tablets to avoid getting sick with withdrawal symptoms.
Physical dependence is not the same as drug addiction. Your healthcare provider can tell you more about the differences between physical dependence and drug addiction.

Clonazepam tablets are a federal controlled substance (C-IV) because it can be abused or lead to dependence. Keep clonazepam tablets in a safe place to prevent misuse and abuse. Selling or giving away clonazepam tablets may harm others, and is against the law. Tell your healthcare provider if you have ever abused or been dependent on alcohol, prescription medicines or street drugs.

What are clonazepam tablets?

Clonazepam tablets are a prescription medicine used alone or with other medicines to treat:

certain types of seizure disorders (epilepsy) in adults and children
panic disorder with or without fear of open spaces (agoraphobia) in adults

It is not known if clonazepam tablets are safe or effective in treating panic disorder in children younger than 18 years old.

Who should not take clonazepam tablets?

Do not take clonazepam tablets if you:

are allergic to benzodiazepines
have significant liver disease
have an eye disease called acute narrow angle glaucoma

Ask your healthcare provider if you are not sure if you have any of the problems listed above.

Before you take clonazepam tablets, tell your healthcare provider if you:

have liver or kidney problems
have lung problems (respiratory disease)
have or have had depression, mood problems, or suicidal thoughts or behavior
have any other medical problems
are pregnant or plan to become pregnant. It is not known if clonazepam tablets can harm your unborn baby. Tell your healthcare provider right away if you become pregnant while taking clonazepam tablets. You and your healthcare provider will decide if you should take clonazepam tablets while you are pregnant.
Studies in pregnant animals have shown harmful effects of benzodiazepine medications (including the active ingredient in clonazepam tablets) on the developing fetus.
Children born to mothers receiving benzodiazepine medications (including clonazepam tablets) late in pregnancy may be at some risk of experiencing breathing problems, feeding problems, hypothermia, and withdrawal symptoms.
If you become pregnant while taking clonazepam tablets, talk to your healthcare provider about registering with the North American Antiepileptic Drug Pregnancy Registry. You can register by calling 1-888-233-2334. The purpose of this registry is to collect information about the safety of antiepileptic drugs during pregnancy.
are breastfeeding or plan to breastfeed. Clonazepam can pass into breast milk. You and your healthcare provider should decide how you will feed your baby while you take clonazepam tablets.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Taking clonazepam tablets with certain other medicines can cause side effects or affect how well clonazepam tablets or the other medicines work. Do not start or stop other medicines without talking to your healthcare provider.

How should I take clonazepam tablets?

Take clonazepam tablets exactly as your healthcare provider tells you. If you take clonazepam tablets for seizures, your healthcare provider may change the dose until you are taking the right amount of medicine to control your symptoms.
Clonazepam is available as a tablet.
Do not stop taking clonazepam tablets without first talking to your healthcare provider. Stopping clonazepam tablets suddenly can cause serious problems.
Clonazepam tablets should be taken with water and swallowed whole.
If you take too many clonazepam tablets, call your healthcare provider or local Poison Control Center right away.

What should I avoid while taking clonazepam tablets?

Clonazepam tablets can slow your thinking and motor skills. Do not drive, operate heavy machinery, or do other dangerous activities until you know how clonazepam tablets affect you.
Do not drink alcohol or take other medicines that may make you sleepy or dizzy while taking clonazepam tablets until you talk to your healthcare provider. When taken with alcohol or medicines that cause sleepiness or dizziness, clonazepam tablets may make your sleepiness or dizziness worse.

What are the possible side effects of clonazepam tablets?

See “What is the most important information I should know about clonazepam tablets?”

Clonazepam tablets can also make your seizures happen more often or make them worse. Call your healthcare provider right away if your seizures get worse while taking clonazepam tablets.

The most common side effects of clonazepam tablets include:

drowsiness
problems with walking and coordination
dizziness
depression
fatigue
problems with memory

These are not all the possible side effects of clonazepam tablets. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Teva Pharmaceuticals USA, Inc. at 1-888-838-2872.

How should I store clonazepam tablets?

Store clonazepam tablets between 68° to 77°F (20° to 25°C)
Keep clonazepam tablets and all medicines out of the reach of children

General Information about the safe and effect use of clonazepam tablets

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use clonazepam tablets for a condition for which they were not prescribed. Do not give clonazepam tablets to other people, even if they have the same symptoms that you have. They may harm them.

You can ask your pharmacist or healthcare provider for information about clonazepam tablets that is written for health professionals.

What are the ingredients in clonazepam tablets USP?

Active ingredient: clonazepam, USP

Inactive ingredients:

0.5 mg tablets contain corn starch, lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone, and Yellow D&C No. 10 Aluminum Lake
1 mg tablets contain corn starch, FD&C Blue No. 1 Aluminum Lake, lactose monohydrate, magnesium

stearate, microcrystalline cellulose, povidone, and Yellow D&C No. 10 Aluminum Lake
2 mg tablets contain corn starch, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and povidone

Manufactured In Israel By:
Teva Pharmaceutical Ind. Ltd.
Jerusalem, 9777402, Israel

Manufactured For:
Teva Pharmaceuticals USA, Inc.
North Wales, PA 19454

For more information, call 1-888-838-2872.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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Indications and Usage

Seizure Disorders

Clonazepam tablets USP are useful alone or as an adjunct in the treatment of the Lennox-Gastaut syndrome (petit mal variant), akinetic and myoclonic seizures. In patients with absence seizures (petit mal) who have failed to respond to succinimides, clonazepam tablets USP may be useful.

In some studies, up to 30% of patients have shown a loss of anticonvulsant activity, often within 3 months of administration. In some cases, dosage adjustment may reestablish efficacy.

Panic Disorder

Clonazepam tablts USP are indicated for the treatment of panic disorder, with or without agoraphobia, as defined in DSM-IV. Panic disorder is characterized by the occurrence of unexpected panic attacks and associated concern about having additional attacks, worry about the implications or consequences of the attacks, and/or a significant change in behavior related to the attacks.

The efficacy of clonazepam tablets USP was established in two 6 to 9 week trials in panic disorder patients whose diagnoses corresponded to the DSM-IIIR category of panic disorder (see CLINICAL PHARMACOLOGY, Clinical Trials).

Panic disorder (DSM-IV) is characterized by recurrent unexpected panic attacks, i.e., a discrete period of intense fear or discomfort in which four (or more) of the following symptoms develop abruptly and reach a peak within 10 minutes: (1) palpitations, pounding heart or accelerated heart rate; (2) sweating; (3) trembling or shaking; (4) sensations of shortness of breath or smothering; (5) feeling of choking; (6) chest pain or discomfort; (7) nausea or abdominal distress; (8) feeling dizzy, unsteady, lightheaded or faint; (9) derealization (feelings of unreality) or depersonalization (being detached from oneself); (10) fear of losing control; (11) fear of dying; (12) paresthesias (numbness or tingling sensations); (13) chills or hot flushes.

The effectiveness of clonazepam tablets USP in long-term use, that is, for more than 9 weeks, has not been systematically studied in controlled clinical trials. The physician who elects to use clonazepam tablets USP for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient (see DOSAGE AND ADMINISTRATION).

Contraindications

Clonazepam should not be used in patients with a history of sensitivity to benzodiazepines, nor in patients with clinical or biochemical evidence of significant liver disease. It may be used in patients with open angle glaucoma who are receiving appropriate therapy but is contraindicated in acute narrow

angle glaucoma.

Warnings

Interference With Cognitive and Motor Performance

Since clonazepam produces CNS depression, patients receiving this drug should be cautioned against engaging in hazardous occupations requiring mental alertness, such as operating machinery or driving a motor vehicle. They should also be warned about the concomitant use of alcohol or other CNS-depressant drugs during clonazepam therapy (see PRECAUTIONS, Drug Interactions and Information for Patients).

Suicidal Behavior and Ideation

Antiepileptic drugs (AEDs), including clonazepam, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

Pooled analyses of 199 placebo-controlled clinical trials (mono- and adjunctive therapy) of 11 different AEDs showed that patients randomized to one of the AEDs had approximately twice the risk (adjusted Relative Risk 1.8, 95% CI:1.2, 2.7) of suicidal thinking or behavior compared to patients randomized to placebo. In these trials, which had a median treatment duration of 12 weeks, the estimated incidence rate of suicidal behavior or ideation among 27,863 AED-treated patients was 0.43% compared to 0.24% among 16,029 placebo-treated patients, representing an increase of approximately one case of suicidal thinking or behavior for every 530 patients treated. There were four suicides in drug-treated patients in the trials and none in placebo-treated patients, but the number is too small to allow any conclusion about drug effect on suicide.

The increased risk of suicidal thoughts or behavior with AEDs was observed as early as one week after starting drug treatment with AEDs and persisted for the duration of treatment assessed. Because most trials included in the analysis did not extend beyond 24 weeks, the risk of suicidal thoughts or behavior beyond 24 weeks could not be assessed.

The risk of suicidal thoughts or behavior was generally consistent among drugs in the data analyzed. The finding of increased risk with AEDs of varying mechanisms of action and across a range of indications suggests that the risk applies to all AEDs used for any indication. The risk did not vary substantially by age (5 to 100 years) in the clinical trials analyzed.

The relative risk for suicidal thoughts or behavior was higher in clinical trials for epilepsy than in clinical trials for psychiatric or other conditions, but the absolute risk differences were similar for the epilepsy and psychiatric indications.

Anyone considering prescribing clonazepam or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.

Pregnancy Risks

Data from several sources raise concerns about the use of clonazepam during pregnancy.

Animal Findings

In three studies in which clonazepam was administered orally to pregnant rabbits at doses of 0.2, 1, 5 or 10 mg/kg/day (low dose approximately 0.2 times the maximum recommended daily human dose of 20 mg/day for seizure disorders and equivalent to the maximum dose of 4 mg/day for panic disorder, on a mg/m2 basis) during the period of organogenesis, a similar pattern of malformations (cleft palate, open eyelid, fused sternebrae and limb defects) was observed in a low, non-dose-related incidence in exposed litters from all dosage groups. Reductions in maternal weight gain occurred at dosages of 5 mg/kg/day or greater and reduction in embryo-fetal growth occurred in one study at a dosage of 10 mg/kg/day. No adverse maternal or embryo-fetal effects were observed in mice and rats following administration during organogenesis of oral doses up to 15 mg/kg/day or 40 mg/kg/day, respectively (4 and 20 times the maximum recommended human dose of 20 mg/day for seizure disorders and 20 and 100 times the maximum dose of 4 mg/day for panic disorder, respectively, on a mg/m2 basis).

General Concerns and Considerations About Anticonvulsants

Recent reports suggest an association between the use of anticonvulsant drugs by women with epilepsy and an elevated incidence of birth defects in children born to these women. Data are more extensive with respect to diphenylhydantoin and phenobarbital, but these are also the most commonly prescribed anticonvulsants; less systematic or anecdotal reports suggest a possible similar association with the use of all known anticonvulsant drugs.

In children of women treated with drugs for epilepsy, reports suggesting an elevated incidence of birth defects cannot be regarded as adequate to prove a definite cause and effect relationship. There are intrinsic methodologic problems in obtaining adequate data on drug teratogenicity in humans; the possibility also exists that other factors (e.g., genetic factors or the epileptic condition itself) may be more important than drug therapy in leading to birth defects. The great majority of mothers on anticonvulsant medication deliver normal infants. It is important to note that anticonvulsant drugs should not be discontinued in patients in whom the drug is administered to prevent seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and threat to life. In individual cases where the severity and frequency of the seizure disorder are such that the removal of medication does not pose a serious threat to the patient, discontinuation of the drug may be considered prior to and during pregnancy; however, it cannot be said with any confidence that even mild seizures do not pose some hazards to the developing embryo or fetus.

General Concerns About Benzodiazepines

An increased risk of congenital malformations associated with the use of benzodiazepine drugs has been suggested in several studies.

There may also be nonteratogenic risks associated with the use of benzodiazepines during pregnancy. There have been reports of neonatal flaccidity, respiratory and feeding difficulties, and hypothermia in children born to mothers who have been receiving benzodiazepines late in pregnancy. In addition, children born to mothers receiving benzodiazepines late in pregnancy may be at some risk of experiencing withdrawal symptoms during the postnatal period.

Advice Regarding the Use of Clonazepam in Women of Childbearing Potential

In general, the use of clonazepam in women of childbearing potential, and more specifically during known pregnancy, should be considered only when the clinical situation warrants the risk to the fetus.

The specific considerations addressed above regarding the use of anticonvulsants for epilepsy in women of childbearing potential should be weighed in treating or counseling these women.

Because of experience with other members of the benzodiazepine class, clonazepam is assumed to be capable of causing an increased risk of congenital abnormalities when administered to a pregnant woman during the first trimester. Because use of these drugs is rarely a matter of urgency in the treatment of panic disorder, their use during the first trimester should almost always be avoided. The possibility that a woman of childbearing potential may be pregnant at the time of institution of therapy should be

considered. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. Patients should also be advised that if they become pregnant during therapy or intend to become pregnant, they should communicate with their physician about the desirability of discontinuing the drug.

Withdrawal Symptoms

Withdrawal symptoms of the barbiturate type have occurred after the discontinuation of benzodiazepines (see DRUG ABUSE AND DEPENDENCE).

Precautions

General

Worsening of Seizures

When used in patients in whom several different types of seizure disorders coexist, clonazepam may increase the incidence or precipitate the onset of generalized tonic-clonic seizures (grand mal). This may require the addition of appropriate anticonvulsants or an increase in their dosages. The concomitant use of valproic acid and clonazepam may produce absence status.

Laboratory Testing During Long-Term Therapy

Periodic blood counts and liver function tests are advisable during long-term therapy with clonazepam.

Risks of Abrupt Withdrawal

The abrupt withdrawal of clonazepam, particularly in those patients on long-term, high-dose therapy, may precipitate status epilepticus. Therefore, when discontinuing clonazepam, gradual withdrawal is essential. While clonazepam is being gradually withdrawn, the simultaneous substitution of another anticonvulsant may be indicated.

Caution in Renally Impaired Patients

Metabolites of clonazepam are excreted by the kidneys; to avoid their excess accumulation, caution should be exercised in the administration of the drug to patients with impaired renal function.

Hypersalivation

Clonazepam may produce an increase in salivation. This should be considered before giving the drug to patients who have difficulty handling secretions. Because of this and the possibility of respiratory depression, clonazepam should be used with caution in patients with chronic respiratory diseases.

Information for Patients

Information for Patients

A clonazepam tablets, USP Medication Guide must be given to the patient each time clonazepam tablets, USP are dispensed, as required by law. Patients should be instructed to take clonazepam only as prescribed. Physicians are advised to discuss the following issues with patients for whom they prescribe clonazepam:

Dose Changes

To assure the safe and effective use of benzodiazepines, patients should be informed that, since benzodiazepines may produce psychological and physical dependence, it is advisable that they consult with their physician before either increasing the dose or abruptly discontinuing this drug.

Interference With Cognitive and Motor Performance

Because benzodiazepines have the potential to impair judgment, thinking or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably

certain that clonazepam therapy does not affect them adversely.

Suicidal Thinking and Behavior

Patients, their caregivers, and families should be counseled that AEDs, including clonazepam, may increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.

Pregnancy

Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy with clonazepam (see WARNINGS, Pregnancy Risks). Patients should be encouraged to enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry if they become pregnant. This registry is collecting information about the safety of antiepileptic drugs during pregnancy. To enroll, patients can call the toll free number 1-888-233-2334 (see PRECAUTIONS, Pregnancy).

Nursing

Patients should be advised not to breastfeed an infant if they are taking clonazepam.

Concomitant Medication

Patients should be advised to inform their physicians if they are taking, or plan to take, any prescription or over-the-counter drugs, since there is a potential for interactions.

Alcohol

Patients should be advised to avoid alcohol while taking clonazepam.

Drug interactions

Effect of Clonazepam on the Pharmacokinetics of Other Drugs

Clonazepam does not appear to alter the pharmacokinetics of phenytoin, carbamazepine or phenobarbital. The effect of clonazepam on the metabolism of other drugs has not been investigated.

Effect of Other Drugs on the Pharmacokinetics of Clonazepam

Literature reports suggest that ranitidine, an agent that decreases stomach acidity, does not greatly alter clonazepam pharmacokinetics.

In a study in which the 2 mg clonazepam orally disintegrating tablet was administered with and without propantheline (an anticholinergic agent with multiple effects on the GI tract) to healthy volunteers, the AUC of clonazepam was 10% lower and the Cmax of clonazepam was 20% lower when the orally disintegrating tablet was given with propantheline compared to when it was given alone.

Fluoxetine does not affect the pharmacokinetics of clonazepam. Cytochrome P-450 inducers, such as phenytoin, carbamazepine and phenobarbital, induce clonazepam metabolism, causing an approximately 30% decrease in plasma clonazepam levels. Although clinical studies have not been performed, based on the involvement of the cytochrome P-450 3A family in clonazepam metabolism, inhibitors of this enzyme system, notably oral antifungal agents, should be used cautiously in patients receiving clonazepam.

Pharmacodynamic Interactions

The CNS-depressant action of the benzodiazepine class of drugs may be potentiated by alcohol, narcotics, barbiturates, nonbarbiturate hypnotics, antianxiety agents, the phenothiazines, thioxanthene and butyrophenone classes of antipsychotic agents, monoamine oxidase inhibitors and the tricyclic antidepressants, and by other anticonvulsant drugs.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been conducted with clonazepam.

The data currently available are not sufficient to determine the genotoxic potential of clonazepam.

In a two-generation fertility study in which clonazepam was given orally to rats at 10 and 100 mg/kg/day (low dose approximately 5 times and 24 times the maximum recommended human dose of 20 mg/day for seizure disorder and 4 mg/day for panic disorder, respectively, on a mg/m2 basis), there was a decrease in the number of pregnancies and in the number of offspring surviving until weaning.

Use in specific populations

Pregnancy

Teratogenic Effects

Pregnancy Category D

(See WARNINGS, Pregnancy Risks).

To provide information regarding the effects of in utero exposure to clonazepam, physicians are advised to recommend that pregnant patients taking clonazepam enroll in the NAAED Pregnancy Registry. This can be done by calling the toll free number 1-888-233-2334, and must be done by patients themselves. Information on this registry can also be found at the website http://www.aedpregnancyregistry.org/.

Labor and Delivery

The effect of clonazepam on labor and delivery in humans has not been specifically studied; however, perinatal complications have been reported in children born to mothers who have been receiving benzodiazepines late in pregnancy, including findings suggestive of either excess benzodiazepine exposure or of withdrawal phenomena (see WARNINGS, Pregnancy Risks).

Nursing Mothers

Mothers receiving clonazepam should not breastfeed their infants.

Pediatric Use

Because of the possibility that adverse effects on physical or mental development could become apparent only after many years, a benefit-risk consideration of the long-term use of clonazepam is important in pediatric patients being treated for seizure disorder (see INDICATIONS AND USAGE and DOSAGE AND ADMINISTRATION).

Safety and effectiveness in pediatric patients with panic disorder below the age of 18 have not been established.

Geriatric Use

Clinical studies of clonazepam did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Because clonazepam undergoes hepatic metabolism, it is possible that liver disease will impair clonazepam elimination. Metabolites of clonazepam are excreted by the kidneys; to avoid their excess accumulation, caution should be exercised in the administration of the drug to patients with impaired renal function. Because elderly patients are more likely to have decreased hepatic and/or renal function, care should be taken in dose selection, and it may be useful to assess hepatic and/or renal function at the

time of dose selection.

Sedating drugs may cause confusion and over-sedation in the elderly; elderly patients generally should be started on low doses of clonazepam and observed closely.

Adverse Reactions

The adverse experiences for clonazepam are provided separately for patients with seizure disorders and with panic disorder.

Seizure Disorders

The most frequently occurring side effects of clonazepam are referable to CNS depression. Experience in treatment of seizures has shown that drowsiness has occurred in approximately 50% of patients and ataxia in approximately 30%. In some cases, these may diminish with time; behavior problems have been noted in approximately 25% of patients. Others, listed by system, are:

Neurologic: Abnormal eye movements, aphonia, choreiform movements, coma, diplopia, dysarthria, dysdiadochokinesis, “glassy-eyed” appearance, headache, hemiparesis, hypotonia, nystagmus, respiratory depression, slurred speech, tremor, vertigo

Psychiatric: Confusion, depression, amnesia, hallucinations, hysteria, increased libido, insomnia, psychosis (the behavior effects are more likely to occur in patients with a history of psychiatric disturbances). The following paradoxical reactions have been observed: excitability, irritability, aggressive behavior, agitation, nervousness, hostility, anxiety, sleep disturbances, nightmares and vivid dreams

Respiratory: Chest congestion, rhinorrhea, shortness of breath, hypersecretion in upper respiratory passages

Cardiovascular: Palpitations

Dermatologic: Hair loss, hirsutism, skin rash, ankle and facial edema

Gastrointestinal: Anorexia, coated tongue, constipation, diarrhea, dry mouth, encopresis, gastritis, increased appetite, nausea, sore gums

Genitourinary: Dysuria, enuresis, nocturia, urinary retention

Musculoskeletal: Muscle weakness, pains

Miscellaneous: Dehydration, general deterioration, fever, lymphadenopathy, weight loss or gain

Hematopoietic: Anemia, leukopenia, thrombocytopenia, eosinophilia

Hepatic: Hepatomegaly, transient elevations of serum transaminases and alkaline phosphatase

Panic Disorder

Adverse events during exposure to clonazepam were obtained by spontaneous report and recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of events into a smaller number of standardized event categories. In the tables and tabulations that follow, CIGY dictionary terminology has been used to classify reported adverse events, except in certain cases in which redundant terms were collapsed into more meaningful terms, as noted below.

The stated frequencies of adverse events represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment-emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation.

Drug Abuse and Dependence

Controlled Substance Class

Clonazepam is a Schedule IV controlled substance.

Physical and Psychological Dependence

Withdrawal symptoms, similar in character to those noted with barbiturates and alcohol (e.g., convulsions, psychosis, hallucinations, behavioral disorder, tremor, abdominal and muscle cramps) have occurred following abrupt discontinuance of clonazepam. The more severe withdrawal symptoms have usually been limited to those patients who received excessive doses over an extended period of time. Generally milder withdrawal symptoms (e.g., dysphoria and insomnia) have been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic levels for several months. Consequently, after extended therapy, abrupt discontinuation should generally be avoided and a gradual dosage tapering schedule followed (see DOSAGE AND ADMINISTRATION). Addiction-prone individuals (such as drug addicts or alcoholics) should be under careful surveillance when receiving clonazepam or other psychotropic agents because of the predisposition of such patients to habituation and dependence.

Following the short-term treatment of patients with panic disorder in Studies 1 and 2 (see CLINICAL PHARMACOLOGY, Clinical Trials), patients were gradually withdrawn during a 7 week downward-titration (discontinuance) period. Overall, the discontinuance period was associated with good tolerability and a very modest clinical deterioration, without evidence of a significant rebound phenomenon. However, there are not sufficient data from adequate and well-controlled long-term clonazepam studies in patients with panic disorder to accurately estimate the risks of withdrawal symptoms and dependence that may be associated with such use.

Overdosage

Human Experience

Symptoms of clonazepam overdosage, like those produced by other CNS depressants, include somnolence, confusion, coma and diminished reflexes.

Overdose Management

Treatment includes monitoring of respiration, pulse and blood pressure, general supportive measures and immediate gastric lavage. Intravenous fluids should be administered and an adequate airway maintained. Hypotension may be combated by the use of levarterenol or metaraminol. Dialysis is of no known value.

Flumazenil, a specific benzodiazepine-receptor antagonist, is indicated for the complete or partial reversal of the sedative effects of benzodiazepines and may be used in situations when an overdose with a benzodiazepine is known or suspected. Prior to the administration of flumazenil, necessary measures should be instituted to secure airway, ventilation and intravenous access. Flumazenil is intended as an adjunct to, not as a substitute for, proper management of benzodiazepine overdose. 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.

Dosage and Administration

Clonazepam tablets USP should be administered with water by swallowing the tablet whole.

Seizure Disorders

Adults

The initial dose for adults with seizure disorders should not exceed 1.5 mg/day divided into three doses. Dosage may be increased in increments of 0.5 to 1 mg every 3 days until seizures are adequately controlled or until side effects preclude any further increase. Maintenance dosage must be individualized for each patient depending upon response. Maximum recommended daily dose is 20 mg.

The use of multiple anticonvulsants may result in an increase of depressant adverse effects. This should be considered before adding clonazepam to an existing anticonvulsant regimen.

Pediatric Patients

Clonazepam is administered orally. In order to minimize drowsiness, the initial dose for infants and children (up to 10 years of age or 30 kg of body weight) should be between 0.01 and 0.03 mg/kg/day but not to exceed 0.05 mg/kg/day given in two or three divided doses. Dosage should be increased by no more than 0.25 to 0.5 mg every third day until a daily maintenance dose of 0.1 to 0.2 mg/kg of body weight has been reached, unless seizures are controlled or side effects preclude further increase. Whenever possible, the daily dose should be divided into three equal doses. If doses are not equally divided, the largest dose should be given before retiring.

Geriatric Patients

There is no clinical trial experience with clonazepam in seizure disorder patients 65 years of age and older. In general, elderly patients should be started on low doses of clonazepam and observed closely (see PRECAUTIONS, Geriatric Use).

Panic Disorder

Adults

The initial dose for adults with panic disorder is 0.25 mg bid. An increase to the target dose for most patients of 1 mg/day may be made after 3 days. The recommended dose of 1 mg/day is based on the results from a fixed dose study in which the optimal effect was seen at 1 mg/day. Higher doses of 2, 3 and 4 mg/day in that study were less effective than the 1 mg/day dose and were associated with more adverse effects. Nevertheless, it is possible that some individual patients may benefit from doses of up to a maximum dose of 4 mg/day, and in those instances, the dose may be increased in increments of 0.125 to 0.25 mg bid every 3 days until panic disorder is controlled or until side effects make further increases undesired. To reduce the inconvenience of somnolence, administration of one dose at bedtime may be desirable.

Treatment should be discontinued gradually, with a decrease of 0.125 mg bid every 3 days, until the drug is completely withdrawn.

There is no body of evidence available to answer the question of how long the patient treated with clonazepam should remain on it. Therefore, the physician who elects to use clonazepam for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient.

Pediatric Patients

There is no clinical trial experience with clonazepam in panic disorder patients under 18 years of age.

Geriatric Patients

There is no clinical trial experience with clonazepam in panic disorder patients 65 years of age and older. In general, elderly patients should be started on low doses of clonazepam and observed closely (see PRECAUTIONS, Geriatric Use).

Online drug information

To view the manufacturer's complete drug information please visit the FDA site:

http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=1617e8e2-54a8-4119-b865-d20d2350df3e

Label

NDC: 51655-865-52

Clonazepam 1MG CIV

30 Tablets

Lot: Exp: Rx Only

Store at 20C to 25C (68-77F)

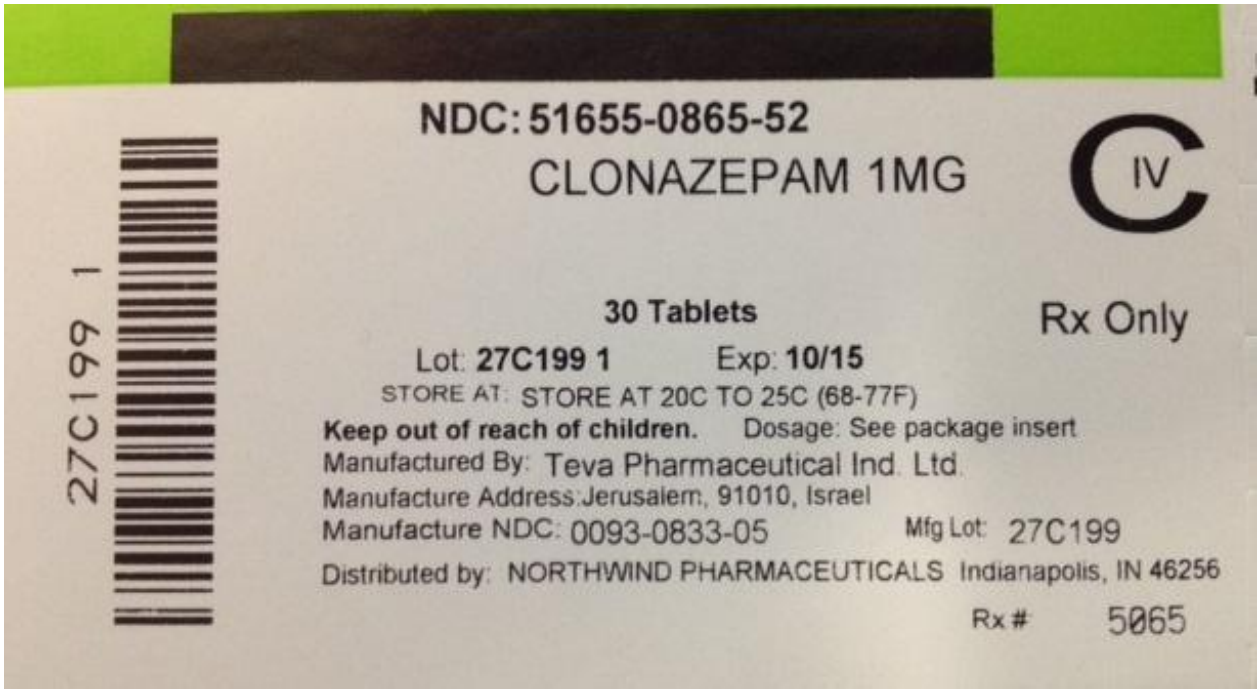
Keep out of reach of children. Dosage: See package insert

Manufactured by: Teva Pharmaceuticals Ind Ltd.

Manufacture Address: Jerusalem, 91010, Israel

Manufacture NDC: 0093-0833-05 Mfg lot:

Distributed by Northwind Pharmaceuticals, Indianapolis, IN 46256



CLONAZEPAM

clonazepam tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:51655-865(NDC:0093-0833)
Route of Administration	ORAL	**DEA Schedule**	CIV

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CLONAZEPAM (UNII: 5PE9FDE8GB) (CLONAZEPAM - UNII:5PE9FDE8GB)	CLONAZEPAM	1 mg

Product Characteristics

Color	green	**Score**	2 pieces
Shape	ROUND	**Size**	8mm
Flavor		**Imprint Code**	833;TEVA
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:51655-865-52	30 in 1 BOTTLE, DISPENSING; Type 0: Not a Combination Product	06/01/2014	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA074569	06/01/2014	

Labeler - Northwind Pharmaceuticals (036986393)

Registrant - Northwind Pharmaceuticals (036986393)

Establishment

Name	Address	ID/FEI	Business Operations
EPM Packaging		079124340	repack(51655-865)

Revised: 9/2018 Northwind Pharmaceuticals