

**CHLORDIAZEPOXIDE HYDROCHLORIDE AND CLIDINIUM BROMIDE-  
chlordiazepoxide hydrochloride and clidinium bromide capsule  
American Health Packaging**

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**Chlordiazepoxide Hydrochloride and Clidinium Bromide Capsules, USP  
Rx Only  
8463994/1121F**

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

- **Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of these drugs in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients for signs and symptoms of respiratory depression and sedation (see WARNINGS and PRECAUTIONS and PRECAUTIONS, Drug Interactions).**
- **The use of benzodiazepines, including chlordiazepoxide hydrochloride, a component of Chlordiazepoxide hydrochloride and clidinium bromide capsules, USP, 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 Chlordiazepoxide hydrochloride and clidinium bromide capsules, USP and throughout treatment, assess each patient's risk for abuse, misuse, and addiction (see WARNINGS).**
- **The continued use of benzodiazepines, including Chlordiazepoxide hydrochloride and clidinium bromide capsules, USP, 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 Chlordiazepoxide hydrochloride and clidinium bromide capsules, USP 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 Chlordiazepoxide hydrochloride and clidinium bromide capsules, USP or reduce the dosage (see WARNINGS and DOSAGE AND ADMINISTRATION).**

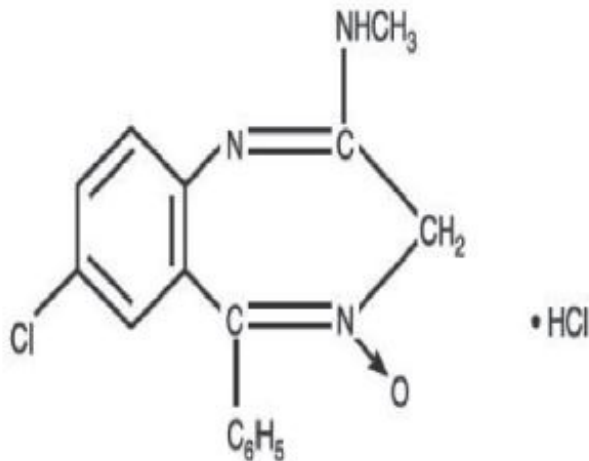
**DESCRIPTION**

Chlordiazepoxide hydrochloride and clidinium bromide capsules, USP is a fixed-combination of chlordiazepoxide hydrochloride, a benzodiazepine, and clidinium bromide, an anticholinergic.

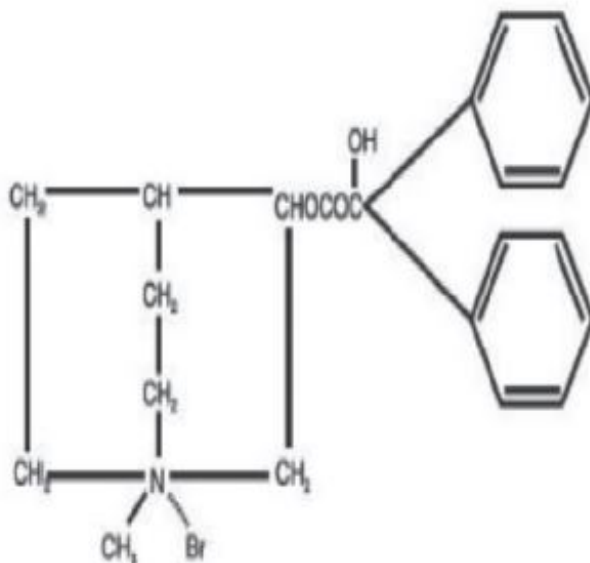
Each chlordiazepoxide hydrochloride and clidinium bromide capsules, USP contains the active ingredients 5 mg chlordiazepoxide hydrochloride and 2.5 mg clidinium bromide.

Each capsule also contains the inactive ingredients lactose monohydrate, maize starch, talc, D&C Yellow No. 10, FD&C Blue No. 1, titanium dioxide, gelatin, shellac, propylene glycol, black iron oxide and potassium hydroxide.

Chlordiazepoxide hydrochloride is 7-Chloro-2-(methylamino)-5-phenyl-3H-1, 4-benzodiazepine 4-oxide monohydrochloride. A colorless, crystalline substance, it is soluble in water. It is unstable in solution and the powder must be protected from light. The molecular weight is 336.22. The structural formula of chlordiazepoxide hydrochloride is as follows:



Clidinium bromide is a synthetic anticholinergic agent which has been shown in experimental and clinical studies to have an antispasmodic and antisecretory effects on the gastrointestinal tract. Structurally clidinium bromide is:



## **ANIMAL PHARMACOLOGY**

Chlordiazepoxide hydrochloride has been studied extensively in many species of animals and these studies are suggestive of action on the limbic system of the brain, which recent evidence indicates is involved in emotional responses. Hostile monkeys were made tame by oral drug doses, which did not cause sedation. Chlordiazepoxide hydrochloride revealed a "taming-action with the elimination of fear and aggression". The taming effect of chlordiazepoxide hydrochloride was further demonstrated in rats made vicious by lesions in the septal area of the brain. The drug dosage which effectively blocked the vicious reaction was well below the dose which caused sedation in these animals.

The oral LD<sub>50</sub> of single doses of chlordiazepoxide hydrochloride, calculated according to the method of Miller and Tainter, is  $720 \pm 51$  mg/kg as 50 determined in mice observed over a period of 5 days following dosage.

Clidinium bromide is an effective anticholinergic agent with activity approximating that of atropine sulfate against acetylcholine-induced spasms in isolated intestinal strips. On oral administration in mice, it proved an effective antisialagogue in preventing pilocarpine-induced salivation. Spontaneous intestinal motility in both rats and dogs is reduced following oral dosing with 0.1 to 0.25 mg/kg. Potent cholinergic ganglionic blocking effects (vagal) were produced with intravenous usage in anesthetized dogs.

Oral doses of 2.5 mg/kg to dogs produced signs of nasal dryness and slight pupillary dilation. In two other species, monkeys and rabbits, doses of 5 mg/kg, po, given three times daily for 5 days did not produce apparent secretory or visual changes.

The oral LD of single doses of clidinium bromide is  $860 \pm 57$  mg/kg as determined in mice observed over a period of 5 days following dosage; the 50 calculations were made according to the method of Miller and Tainter.

### *Effects on Reproduction:*

Reproduction studies in rats fed chlordiazepoxide hydrochloride, 10, 20 and 80 mg/kg daily, and bred through one or two matings showed no congenital anomalies, nor were there adverse effects on lactation of the dams or growth of the newborn. However, in another study at 100 mg/kg daily there was noted a significant decrease in the fertilization rate and a marked decrease in the viability and body weight of offspring which may be attributable to sedative activity, thus resulting in lack of interest in mating and lessened maternal nursing and care of the young. One neonate in each of the first and second matings in the rat reproduction study at the 100 mg/kg dose exhibited major skeletal defects. Further studies are in progress to determine the significance of these findings.

Two series of reproduction experiments with clidinium bromide were carried out in rats, employing dosages of 2.5 and 10 mg/kg daily in each experiment. In the first experiment, clidinium bromide was administered for a 9-week interval prior to mating; no untoward effect on fertilization or gestation was noted. The offspring were taken by caesarean section and did not show a significant incidence of congenital anomalies when compared to control animals. In the second experiment, adult animals were given clidinium bromide for 10 days prior to and through two mating cycles. No significant effects were observed on fertility, gestation, viability of offspring or lactation, as compared to control animals, nor was there a significant incidence of congenital anomalies in the offspring derived from these experiments.

A reproduction study of chlordiazepoxide hydrochloride and clidinium bromide capsules was carried out in rats through two successive matings. Oral daily doses were administered in two concentrations: 2.5 mg/kg chlordiazepoxide hydrochloride with 1.25 mg/kg clidinium bromide or 25 mg/kg chlordiazepoxide hydrochloride with 12.5 mg/kg clidinium bromide. In the first mating, no significant differences were noted between the control or the treated groups, with the exception of a slight decrease in the number of animals surviving during lactation among those receiving the highest dosage. As with all anticholinergic drugs, an inhibiting effect on lactation may occur. In the second mating, similar results were obtained except for a slight decrease in the number of pregnant females and in the percentage of offspring surviving until weaning. No congenital anomalies were observed in both matings in either the control or treated groups. Additional animal reproduction studies are in progress.

## **INDICATIONS AND USAGE**

Chlordiazepoxide hydrochloride and clidinium bromide capsules is indicated to control emotional and somatic factors in gastrointestinal disorders. Chlordiazepoxide hydrochloride and clidinium bromide capsules may also be used as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

## **CONTRAINDICATIONS**

Chlordiazepoxide hydrochloride and clidinium bromide capsules is contraindicated in the presence of glaucoma (since the anticholinergic component may produce some degree of mydriasis) and in patients with prostatic hypertrophy and benign bladder neck obstruction. It is contraindicated in patients with known hypersensitivity to chlordiazepoxide hydrochloride and/or clidinium bromide.

## **WARNINGS**

### **Risks From Concomitant Use with Opioids**

Concomitant use of benzodiazepines, including chlordiazepoxide hydrochloride and clidinium bromide capsules and opioids may result in profound sedation, respiratory depression, coma, and death. Because of these risks, reserve concomitant prescribing of these drugs- in patients for whom alternative treatment options are inadequate.

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. If a decision is made to prescribe chlordiazepoxide hydrochloride and clidinium bromide capsules concomitantly with opioids, prescribe the lowest effective dosages and minimum durations of concomitant use, and follow patients closely for signs and symptoms of respiratory depression and sedation. Advise both patients and caregivers about the risks of respiratory depression and sedation when chlordiazepoxide hydrochloride and clidinium bromide capsules is used with opioids (see **PRECAUTIONS**).

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

The use of benzodiazepines, including chlordiazepoxide hydrochloride, a component of

chlordiazepoxide hydrochloride and clidinium bromide capsules, 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**).

Before prescribing chlordiazepoxide hydrochloride and clidinium bromide capsules and throughout treatment, assess each patient's risk for abuse, misuse, and addiction (e.g., using a standardized screening tool). Use of chlordiazepoxide hydrochloride and clidinium bromide capsules, particularly in patients at elevated risk, necessitates counseling about the risks and proper use of chlordiazepoxide hydrochloride and clidinium bromide capsules 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 chlordiazepoxide hydrochloride and clidinium bromide capsules or reduce the dosage (a patient-specific plan should be used to taper the dosage) (see **DOSAGE AND ADMINISTRATION**).

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 chlordiazepoxide hydrochloride and clidinium bromide capsules, may lead to clinically significant physical dependence. Abrupt discontinuation or rapid dosage reduction of chlordiazepoxide hydrochloride and clidinium bromide 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**).

#### 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**).

### **Effects on the Ability to Drive or Operate Machinery**

As in the case of other preparations containing CNS-acting drugs, patients receiving chlordiazepoxide hydrochloride and clidinium bromide capsules should be cautioned about possible combined effects with opioids, alcohol and other CNS depressants. For the same reason, they should be cautioned against hazardous occupations requiring complete mental alertness, such as operating machinery or driving a motor vehicle.

### **Usage in Pregnancy**

An increased risk of congenital malformations associated with the use of minor tranquilizers (chlordiazepoxide, diazepam and meprobamate) during the first trimester of pregnancy has been suggested in several studies. Because use of these drugs is rarely a matter of urgency, their use during this period 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. Patients should be advised that if they become pregnant during therapy or intend to become pregnant they should communicate with their physicians about the desirability of discontinuing the drug.

As with all anticholinergic drugs, an inhibiting effect on lactation may occur (see **ANIMAL PHARMACOLOGY**).

## **OVERDOSAGE**

Manifestations of chlordiazepoxide hydrochloride overdosage include somnolence, confusion, coma and diminished reflexes. Respiration, pulse and blood pressure should be monitored, as in all cases of drug overdosage, although, in general, these effects have been minimal following chlordiazepoxide hydrochloride overdosage.

While the signs and symptoms of chlordiazepoxide hydrochloride and clidinium bromide capsules overdosage may be produced by either of its components, usually such symptoms will be overshadowed by the anticholinergic actions of clidinium bromide. The symptoms of overdosage of clidinium bromide are excessive dryness of mouth, blurring of vision, urinary hesitancy and constipation.

General supportive measures should be employed, along with immediate gastric lavage. Administer physostigmine 0.5 to 2 mg at a rate of no more than 1 mg per minute. This may be repeated in 1 to 4 mg doses if arrhythmias, convulsions or deep coma recur. Intravenous fluids should be administered and an adequate airway maintained. Hypotension may be combated by the use of levarterenol or metaraminol. Methylphenidate or caffeine and sodium benzoate may be given to combat CNS-depressive effects. Dialysis is of limited value. Should excitation occur, barbiturates should not be used. As with the management of intentional overdosage with any drug, it should be borne in mind that multiple agents may have been ingested.

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

## **PRECAUTIONS**

### **CNS Adverse Reactions**

In geriatric or debilitated patients, it is recommended that the dosage be limited to the smallest effective amount to preclude the development of ataxia, oversedation or confusion (not more than 2 chlordiazepoxide hydrochloride and clidinium bromide capsules, capsules per day initially, to be increased gradually as needed and tolerated). In general, the concomitant administration of chlordiazepoxide hydrochloride and clidinium bromide capsules and other psychotropic agents is not recommended. If such combination therapy seems indicated, careful consideration should be given to the pharmacology of the agents to be employed – particularly when the known potentiating compounds such as the MAO inhibitors and phenothiazines are to be used. The usual

precautions in treating patients with impaired renal or hepatic function should be observed.

Paradoxical reactions to chlordiazepoxide hydrochloride, e.g., excitement, stimulation and acute rage, have been reported in psychiatric patients and should be watched for during chlordiazepoxide hydrochloride and clidinium bromide capsules therapy. The usual precautions are indicated when chlordiazepoxide hydrochloride is used in the treatment of anxiety states where there is any evidence of impending depression; it should be borne in mind that suicidal tendencies may be present and protective measures may be necessary.

## **Information for Patients**

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

Inform patients that the use of chlordiazepoxide hydrochloride and clidinium bromide capsules, 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**).

### **Withdrawal Reactions**

Inform patients that the continued use of chlordiazepoxide hydrochloride and clidinium bromide capsules may lead to clinically significant physical dependence and that abrupt discontinuation or rapid dosage reduction of chlordiazepoxide hydrochloride and clidinium bromide capsules 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 chlordiazepoxide hydrochloride and clidinium bromide capsules may require a slow taper (see **WARNINGS and DRUG ABUSE AND DEPENDENCE**).

### **Concomitant Use With Opioids and Other CNS Depressants**

Inform patients and caregivers that potentially fatal additive effects may occur if chlordiazepoxide hydrochloride and clidinium bromide capsules is used with opioids or other CNS depressants, including alcohol, and not to use these concomitantly unless supervised by a health care provider (see **WARNINGS and PRECAUTIONS, Drug Interactions**).

## **Drug Interactions**

### **Opioids**

The concomitant use of benzodiazepines, including chlordiazepoxide hydrochloride, a component of chlordiazepoxide hydrochloride and clidinium bromide capsules, and opioids increases the risk of respiratory depression because of actions at different receptor sites in the CNS that control respiration.

Benzodiazepines interact at GABAA sites and opioids interact primarily at mu receptors. When benzodiazepines and opioids are combined, the potential for benzodiazepines to significantly worsen opioid-related respiratory depression exists. Limit dosage and duration of concomitant use of chlordiazepoxide hydrochloride and clidinium bromide capsules and opioids, and follow patients closely for respiratory depression and

sedation.

### Oral Anticoagulants

Although clinical studies have not established a cause and effect relationship, physicians should be aware that variable effects on blood coagulation have been reported very rarely in patients receiving oral anticoagulants and chlordiazepoxide hydrochloride, a component of chlordiazepoxide hydrochloride and clidinium bromide capsules.

### **Pediatric Use**

Safety and effectiveness in pediatric patients have not been established.

### **Geriatric Use**

Geriatric subjects may be particularly prone to experiencing drowsiness, ataxia and confusion while receiving chlordiazepoxide hydrochloride and clidinium bromide capsules. These effects can usually be avoided with proper dosage adjustment, although they have occasionally been observed even at the lower dosage ranges. Dosing in geriatric subjects should be initiated cautiously (no more than 2 capsules per day) and increased gradually if needed and tolerated (see **DOSAGE AND ADMINISTRATION**). chlordiazepoxide hydrochloride and clidinium bromide capsules is contraindicated in the presence of glaucoma, prostatic hypertrophy and benign bladder neck obstruction (see **CONTRAINDICATIONS**).

### **ADVERSE REACTIONS**

No side effects or manifestations not seen with either compound alone have been reported with the administration of chlordiazepoxide hydrochloride and clidinium bromide capsules. However, since chlordiazepoxide hydrochloride and clidinium bromide capsules contains chlordiazepoxide hydrochloride and clidinium bromide, the possibility of untoward effects which may be seen with either of these two compounds cannot be excluded.

When chlordiazepoxide hydrochloride has been used alone the necessity of discontinuing therapy because of undesirable effects has been rare. Drowsiness, ataxia and confusion have been reported in some patients — particularly the elderly and debilitated. While these effects can be avoided in almost all instances by proper dosage adjustment, they have occasionally been observed at the lower dosage ranges. In a few instances syncope has been reported.

Other adverse reactions reported during therapy with chlordiazepoxide hydrochloride include isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, as well as increased and decreased libido. Such side effects have been infrequent and are generally controlled with reduction of dosage. Changes in EEG patterns (low-voltage fast activity) have been observed in patients during and after chlordiazepoxide hydrochloride treatment.

Blood dyscrasias, including agranulocytosis, jaundice and hepatic dysfunction have occasionally been reported during therapy with chlordiazepoxide hydrochloride. When chlordiazepoxide hydrochloride treatment is protracted, periodic blood counts and liver function tests are advisable.

Adverse effects reported with use of chlordiazepoxide hydrochloride and clidinium



bromide capsules are those typical of anticholinergic agents, i.e., dryness of the mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when chlordiazepoxide hydrochloride and clidinium bromide capsules therapy has been combined with other spasmolytic agents and/or a low residue diet.

**To report SUSPECTED ADVERSE REACTIONS, contact Ascend Laboratories, LLC at 1-877-ASC-RX01 (877-272-7901) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

## **DRUG ABUSE AND DEPENDENCE**

### **Controlled Substance**

Chlordiazepoxide hydrochloride and clidinium bromide capsules contains chlordiazepoxide hydrochloride, a Schedule IV controlled substance and clidinium bromide, which is not a controlled substance. Chlordiazepoxide hydrochloride and clidinium bromide capsules is exempted from Schedule IV and is not controlled under the Controlled Substances Act.

### **Abuse**

Chlordiazepoxide hydrochloride, a component of chlordiazepoxide hydrochloride and clidinium bromide capsules, is 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**).

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).

## **Dependence**

### Physical Dependence

Chlordiazepoxide hydrochloride and clidinium bromide capsules 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**).

To reduce the risk of withdrawal reactions, use a gradual taper to discontinue chlordiazepoxide hydrochloride and clidinium bromide capsules or reduce the dosage (see **WARNINGS and DOSAGE AND ADMINISTRATION**).

### 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 chlordiazepoxide hydrochloride and clidinium bromide capsules 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 effects of chlordiazepoxide hydrochloride and clidinium bromide capsules may develop; however, little tolerance develops to the amnestic reactions and other cognitive impairments caused by benzodiazepines.

## **DOSAGE AND ADMINISTRATION**

### **Recommended Dosage**

Because of the varied individual responses to tranquilizers and anticholinergics, the optimum dosage of chlordiazepoxide hydrochloride and clidinium bromide capsules, USP varies with the diagnosis and response of the individual patient. The dosage, therefore, should be individualized for maximum beneficial effects. The usual maintenance dose is 1 or 2 capsules, 3 or 4 times a day administered before meals and at bedtime.

### **Recommended Geriatric Dosage**

Dosage should be limited to the smallest effective amount to preclude the development of ataxia, oversedation or confusion. The initial dose should not exceed 2 chlordiazepoxide hydrochloride and clidinium bromide capsules, USP capsules per day, to be increased gradually as needed and tolerated. Elderly patients have an increased risk of dose-related adverse reactions (see **PRECAUTIONS**).

### **Discontinuation or Dosage Reduction of chlordiazepoxide hydrochloride and clidinium bromide**

To reduce the risk of withdrawal reactions, use a gradual taper to discontinue chlordiazepoxide hydrochloride and clidinium bromide or reduce the dosage. If a patient develops withdrawal reactions, consider pausing the taper or increasing the dosage to the previous tapered dosage level. Subsequently decrease the dosage more slowly (see **WARNINGS and DRUG ABUSE AND DEPENDENCE**).

### **HOW SUPPLIED**

Chlordiazepoxide hydrochloride and clidinium bromide capsules is available in green opaque capsules, each containing 5 mg chlordiazepoxide hydrochloride and 2.5 mg clidinium bromide in

Unit dose packages of 20 (2 x 10) NDC 60687-639-94 with "CDP/CD" imprinted on the cap and 5/2.5" imprinted on the body of the capsule.

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F). [see USP Controlled Room Temperature];

**FOR YOUR PROTECTION:** Do not use if blister is torn or broken.

**Keep out of reach of children.**

### **PACKAGING INFORMATION**

American Health Packaging unit dose blisters (see How Supplied section) contain drug product from Ascend Laboratories, LLC as follows:

(5 mg/2.5 mg / 20 UD) NDC 60687-639-94 packaged from NDC 67877-731

Distributed by:

**American Health Packaging**

Columbus, OH 43217

**8463994/1121F**

**Package/Label Display Panel - Carton - 5 mg/2.5 mg**

NDC 60687-**639**-94

**Chlordiazepoxide Hydrochloride  
and Clidinium Bromide** Capsules, USP

**5 mg/2.5 mg**

20 Capsules (2 x 10)

Rx Only



NDC 60687-**639**-94

**Chlordiazepoxide Hydrochloride  
and Clidinium Bromide**

Capsules, USP

**5 mg/2.5 mg**

**20 Capsules (2 x 10)**

**Rx Only**

**PHARMACIST:** Dispense with the accompanying Medication Guide to each patient.

**DEA EXEMPT PRODUCT**

**Each Capsule Contains:**

5 mg chlordiazepoxide HCl and 2.5 mg clidinium bromide.

**Usual Adult Dosage:** One or two capsules 3 or 4 times a day, before meals and at bedtime. See package insert for additional dosage recommendations and full prescribing information.

**Store** at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

**Keep this and all drugs out of reach of children.**

**FOR YOUR PROTECTION:** Do not use if blister is torn or broken.

The drug product contained in this package is from NDC # 67877-731, Ascend Laboratories, LLC.

Distributed by:  
American Health Packaging  
Columbus, Ohio 43217

763994  
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**Package/Label Display Panel**



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 American Health Packaging  
 Columbus, OH 43217


 Chlordiazepoxide Hydrochloride and Clidinium Bromide Capsule, USP  
**5 mg/2.5 mg**  
 LOT: xxxxxxxx  
 EXPIRY: xx/xx  
 American Health Packaging  
 Columbus, OH 43217

Chlordiazepoxide Hydrochloride and Clidinium Bromide Capsule, USP

**5 mg/2.5 mg**

## CHLORDIAZEPOXIDE HYDROCHLORIDE AND CLIDINIUM BROMIDE

chlordiazepoxide hydrochloride and clidinium bromide capsule

### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:60687-639(NDC:67877-731)
<b>Route of Administration</b>	ORAL	<b>DEA Schedule</b>	CIV

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
<b>CHLORDIAZEPOXIDE HYDROCHLORIDE</b> (UNII: MFM6K1XWDK) (CHLORDIAZEPOXIDE - UNII:6RZ6XEZ3CR)	CHLORDIAZEPOXIDE HYDROCHLORIDE	5 mg

<b>CLIDINIUM BROMIDE</b> (UNII: 91ZQW5JF1Z) (CLIDINIUM - UNII:BO76JF850N)	CLIDINIUM BROMIDE	2.5 mg
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### Inactive Ingredients

Ingredient Name	Strength
<b>LACTOSE MONOHYDRATE</b> (UNII: EWQ57Q8I5X)	
<b>STARCH, CORN</b> (UNII: O8232NY3SJ)	
<b>TALC</b> (UNII: 7SEV7J4R1U)	
<b>D&amp;C YELLOW NO. 10</b> (UNII: 35SW5USQ3G)	
<b>FD&amp;C BLUE NO. 1</b> (UNII: H3R47K3TBD)	
<b>TITANIUM DIOXIDE</b> (UNII: 15FIX9V2JP)	
<b>GELATIN, UNSPECIFIED</b> (UNII: 2G86QN327L)	
<b>SHELLAC</b> (UNII: 46N107B71O)	
<b>PROPYLENE GLYCOL</b> (UNII: 6DC9Q167V3)	
<b>FERROSO FERRIC OXIDE</b> (UNII: XM0M87F357)	
<b>POTASSIUM HYDROXIDE</b> (UNII: WZH3C48M4T)	

### Product Characteristics

<b>Color</b>	green	<b>Score</b>	no score
<b>Shape</b>	CAPSULE	<b>Size</b>	14mm
<b>Flavor</b>		<b>Imprint Code</b>	CDP;CD;5;2;5
<b>Contains</b>			

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60687-639-94	20 in 1 CARTON	01/06/2022	
1	NDC:60687-639-11	1 in 1 BLISTER PACK; Type 0: Not a Combination Product		

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA214065	01/06/2022	

**Labeler** - American Health Packaging (929561009)

### Establishment

Name	Address	ID/FEI	Business Operations
American Health Packaging		929561009	repack(60687-639)