PRESCRIBING INFORMATION

CHLORDIAZEPOXIDE

Chlordiazepoxide HCl Capsules USP

5, 10 and 25 mg

Anxiolytic

AA PHARMA INC.
1165 Creditstone Road Unit #1
Vaughan, Ontario
L4K 4N7

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PHARMACOLOGY

Chlordiazepoxide depresses the CNS at the levels of the cortex, the limbic system, and the brain stem reticular formation, and also depresses polysynaptic reflex arcs of the spinal cord. It does not produce ganglionic blockade or reduce affective responses at therapeutic dosage as do phenothiazine drugs and reserpine; its skeletal muscle relaxant properties are similar to those of meprobamate. Amine oxidase inhibition has not been demonstrated with chlordiazepoxide.

Following oral administration, the drug appears in the blood stream in 0.5 to 1 hour, peak blood levels occur in 2 to 4 hours. After i.m. administration, effects of the drug appear in 15 to 30 minutes. Following administration of radioactive chlordiazepoxide to rats, distribution of the drug or its metabolites has been shown to be fairly even throughout all body tissues. Chlordiazepoxide readily passes the placental barrier, with the concentration of the drug in the fetal circulation approaching or equaling that in maternal circulation. In humans, the plasma half life of a single oral dose of chlordiazepoxide is about 20 to 24 hours. The drug is metabolized, presumable by the liver, to a lactam derivative, which may be further metabolized to the amino acid N-(2-amino-5-chloroalpha-phenylbenzylidine)-glycine-N-oxide. Chlordiazepoxide is excreted, chiefly as the lactam derivative, as the amino acid and conjugates of the amino acid, in the urine and feces.

INDICATIONS

Symptomatic relief of mild anxiety and tension, and for reduction of tension states that may accompany muscle spasm. As an adjunct in tension states associated with insomnia, pre- and post- operative apprehension, tension headache, premenstrual tension and stress, and functional gastrointestinal, cardiovascular, gynecological, and dermatological disorders with an emotional overlay. May be useful in the alleviation of alcohol withdrawal syndromes although drug dependence may result, substituting for alcohol dependence. May also reduce anxiety associated with psychosis, but is not a specific management of psychosis.

CONTRAINDICATIONS

Myasthenia gravis, acute narrow angle glaucoma, known hypersensitivity to benzodiazepines.

PRECAUTIONS

Administer chlordiazepoxide with caution to patients with a history of blood dyscrasias or hepatic or renal disease.

Caution should be exercised and the minimal effective dosage that does not cause ataxia or over-sedation should be maintained in elderly or debilitated patients. Dosage should be increased gradually as needed and tolerated.

Caution patients about engaging in activities requiring mental alertness, judgement and physical co-ordination, such as driving an automobile or operating dangerous machinery.

Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly the use of potentiating drugs such as MAO inhibitors and phenothiazines. Patients should also be warned against the ingestion of alcohol, since tolerance may be decreased and effects enhanced.

Since it has not been found of particular value in psychotic patients, chlordiazepoxide should not be used in place of appropriate treatment.

Drug dependence and withdrawal reactions have been observed; therefore, caution must be exercised in administering the drug to addiction-prone individuals, or to those whose history suggests possible abuse, and in long-term use, treatment should be ceased gradually.

Periodic blood counts and liver function tests are recommended if the medication is administered over a protracted period of time.

Several studies have suggested an increased risk of congenital malformations associated with the use of diazepam, chlordiazepoxide and meprobamate during the first trimester of pregnancy. Therefore, the administration of chlordiazepoxide is rarely justified in women of childbearing potential. If the drug is prescribed for a woman of childbearing potential, she should be warned to contact her physician regarding discontinuation of the drug if she intends to become, or suspects that she is pregnant.

Employ the usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary.

Variable effects on blood coagulation have been reported very rarely in patients

receiving the drug and oral anticoagulants; a casual relationship has not been established clinically.

ADVERSE EFFECTS

Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by the proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances, syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido - all infrequent and generally controlled with dosage reductions; changes in EEG patterns (low voltage fast activity) may appear during and after treatment; blood dyscrasias (including leucopenia and rare cases of agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally. Paradoxical reactions such as excitement, stimulation, elevation of mood, and rage, have been reported in psychotic patients and hyperactive aggressive children.

These reactions may be secondary to the relief of anxiety symptoms and should be watched for particularly in the early phase of medication.

OVERDOSE

Symptoms: Drowsiness, ataxia, confusion. Depression of the cardiovascular and respiratory centres may occur.

Treatment: Gastric lavage or, in children, induce emesis and if there is no immediate response, use gastric lavage. Management consists of supportive measures, close supervision and monitoring. Cardiovascular and CNS stimulants may be used if necessary. Dialysis appears to be of little value. There have been occasional reports of excitation in patients following chlordiazepoxide HC1 overdosage; if this occurs, barbituates 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.

DOSAGE

Individual adjustment of dose is important, with minimum effective dose being used.

Oral: Adults, usually 15 to 40 mg. daily in divided doses. In severe cases 25 mg 3 or 4 times daily may be given. Elderly or debilitated patients 5 mg 2 to 4 times daily. Preoperative apprehension 5 to 10 mg 3 to 4 times daily on days prior to surgery. Obstetrics 25 to 50 mg on admission. Children: Initiate therapy with 5 to 10 mg daily in divided doses, increasing, if necessary, to 30 mg daily in divided doses 2 to 3 times daily.

AVAILABILITY

Each yellow and light green capsule, identified 5 contains 5 mg. Chlordiazepoxide HCl USP.

Each black and light green capsule, identified 10 contains 10 mg. Chlordiazepoxide HCl USP.

Each white and light green capsule, identified 25 contains 25 mg. Chlordiazepoxide HCl USP.

Each strength is available in package size of 100 capsules.