DOXEPIN HYDROCHLORIDE CAPSULES USP

Uses

1. Psychotic depressive disorders with associated anxiety including involutional depression.
2. Psychoneurotic patients with depression and/or anxiety.

At clinical dosages up to 150 mg per day, doxepin HCl can be given to man concomitantly with one or more other antidepressants, or with other psychotropic agents such as tranquilizers or neuroleptics.

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DESCRIPTION

Doxepin hydrochloride is one of a class of psychotherapeutic agents known as tricyclic antidepressants. It is an iminodibenzoxepin tricyclic compound. The molecular formula of the compound is C₂₅H₂₃NO₂Cl.

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CLINICAL PHARMACOLOGY

The mechanism of action of doxepin HCl is not definitely known. It is not a central noradrenergic or serotoninergic agent. In vitro studies have shown that doxepin HCl is a potent inhibitor of the uptake of norepinephrine, 5-hydroxytryptamine, and dopamine into rat brain synaptosomes. Also, in vitro studies have shown that doxepin HCl is a potent inhibitor of the uptake of norepinephrine, 5-hydroxytryptamine, and dopamine into rat brain synaptosomes.

Each doxepin hydrochloride capsule is equivalent to 10 mg, 25 mg, 50 mg, 75 mg, or 100 mg of doxepin for oral administration.

PHARMACOKINETICS

Oral absorption is complete, and plasma levels are proportional to the oral dose, with a half-life of approximately 10 hours. The elimination of doxepin HCl is characterized by a biphasic pattern, with a primary half-life of about 4 hours and a secondary half-life of about 10 hours. The plasma clearance of doxepin HCl is not significantly altered by age or sex and is not affected by significant hepatic or renal impairment. Doxepin HCl is primarily metabolized by CYP2D6 with minor contributions from CYP1A2 and CYP3A4.

The volume of distribution of doxepin HCl is not known. Doxepin HCl is extensively bound to plasma proteins, with a binding affinity of about 95% to plasma albumin. Doxepin HCl is extensively bound to plasma proteins, with a binding affinity of about 95% to plasma albumin.

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WARNINGS.

Sedating drugs may cause confusion and over sedation in the elderly; elderly patients are more likely to have decreased renal function, care should be taken in dose restriction. The extent of renal excretion of doxepin HCl has not been determined. Because elderly patients are more likely to have decreased renal function, care should be taken in dose restriction.

Obtain an ECG and immediately initiate cardiac monitoring. Protect the patient’s airway and respiration. The principles of management of child and adult overdosages are similar. It is strongly recommended that the physician contact the local poison control center for specific advice in tricyclic antidepressant poisoning.

Deaths may occur from overdosage with this class of drugs. Multiple drug ingestion increases the potential for severe toxicity. Physostigmine is not recommended except to treat life-threatening symptoms that are unresponsive to sodium bicarbonate. If these are ineffective, other anticonvulsants (e.g., phenobarbital and phenytoin). Serial arterial blood gases and serum electrolytes should be obtained and monitored. The severity of the overdose. Intravenous sodium bicarbonate should be used to treat metabolic acidosis, which is defined as a arterial pH < 7.3 or a base deficit of at least 6 mmol/L. Exchange transfusion and forced diuresis generally have been reported as ineffective in tricyclic antidepressant poisoning.

In patients with CNS depression, early intubation is advised because of the potential for respiratory depression. Respiratory depression should be considered with electroencephalography, when these data are available. Other anticonvulsants (e.g., phenobarbital and phenytoin) are not recommended except to treat life-threatening symptoms that cannot be managed with supportive therapy alone.

If these are ineffective, other anticonvulsants (e.g., phenobarbital and phenytoin). There are case reports of patients successfully treated with exchange transfusions, and forced diuresis generally have been reported as ineffective in tricyclic antidepressant poisoning.

For most patients with drugs of abuse, medical management is starting, a daily dose of 30 mg is recommended. Physostigmine should be used as the initial dose in adult treatment. The usual dose is 10 to 15 mg in adults and 2 to 5 mg in children. Intravenous sodium bicarbonate should be used to treat metabolic acidosis, which is defined as a arterial pH < 7.3 or a base deficit of at least 6 mmol/L. Exchange transfusion and forced diuresis generally have been reported as ineffective in tricyclic antidepressant poisoning.

In patients with very early electroencephalographic or electrocardiographic abnormalities organic disease, this dosing may be increased. Some of these patients have been given doses as high as 200 to 500 mg daily. The total daily dose of doxepin HCl may be given in a divided or once-daily dosage, depending on the patient's needs. The maximum daily dose is 300 mg.

Antidepressant effects may continue to be apparent for months after the drug has been discontinued. Visual hallucinations, dilated pupils, agitation, hyperactive reflexes, stupor, drowsiness, ataxia, extrapyramidal symptoms, and lethargy have been reported with certain antihistamines, sedatives, hypnotics, ultra-tricyclic antidepressants, and thioxanthenes. Other reported clinical experience has not identified unusual adverse reactions not already included under ADVERSE REACTIONS.

Some of the adverse reactions noted below have not been specifically reported with doxepin HCl but are considered to be within the class.

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