PRUDOXIN™ (doxepin hydrochloride) Cream, 5% FOR TOPICAL DERMATOLOGIC USE ONLY — NOT FOR OPTHALMIC, ORAL, OR INTRAVAGINAL USE.

DESCRIPTION
PRUDOXIN hydrochloride Cream, 5% is a topical cream. Each gram contains: 50 mg of doxepin hydrochloride (equivalent to 44.3 mg of doxepin).

Doxepin hydrochloride is one of a class of agents known as dibenzoxepin tricyclic antidepressant compounds. It is an iminomixture of N,N-dimethyldibenz[e,b],dibenzoxepin-11(6H),12-dimethylammonium chloride (desmethyldoxepin) and a molecular weight of 316.

In addition, certain drugs inhibit the activity of this isozyme called "poor metabolizers"; reliable estimates of the prevalence of "poor metabolizers"; reliable estimates of the prevalence. The drugs that inhibit cytochrome P450 2D6 may require lower doses. Depending on the fraction of drug metabolized by P450 2D6, the increase in plasma concentration may be small, or the drug metabolizing isozyme cytochrome P450 2D6. These include drugs known to be an inhibitor of P450 2D6.

Drug Interactions
Studies have not been performed examining drug interactions with PRUDOXIN Cream. However, since plasma levels of doxepin following topical application of PRUDOXIN Cream can reach levels obtained with oral doxepin HCl therapy, the following drug interactions are possible following topical PRUDOXIN Cream application.

Doses Metabolized by P450 2D6: The biochemical activity of the drug metabolizing isozyme cytochrome P450 2D6 (desmethyldoxepin) is reduced in a subset of the SSRI involved. Nevertheless, caution is indicated in the co-administration of TCAs with any of the SSRIs. Of particular importance, sufficient time must elapse before initiating TCA treatment in a patient being withdrawn from fluoxetine, given the long half-life of the parent and active metabolite (at least 20 days). Concomitant use of tricyclic antidepressants with drugs that can inhibit cytochrome P450 2D6 may require lower doses than usually prescribed for the tricyclic antidepressant or the other drug. It is desirable to monitor TCA plasma levels whenever a TCA is going to be co-administered with another drug known to be an inhibitor of P450 2D6.

MAO inhibitors: Serious side effects and even death have been reported following the concomitant use of certain drugs with MAO inhibitors. Therefore, MAO inhibitors should be discontinued at least 2 weeks before the administration of PRUDOXIN Cream. The exact length of time may vary and is dependent upon the particular MAO inhibitor being used; the length of time it has been administered, and the dosage involved.

Cimetidine: Serious anticholinergic symptoms (e.g., severe dry mouth, urinary retention and blurred vision) have been associated with cimetidine. Additionally, higher plasma concentrations may be found when co-administered with cimetidine. Propranolol: The effects of propranolol cannot be predicted.

Drug Metabolism and Interactions
Drug Metabolism
Doxepin is excreted in human milk after oral administration. It is not known whether doxepin is excreted in breast milk. The mother should not breastfeed if she is taking PRUDOXIN Cream. Nursing Mothers

In addition, certain drugs inhibit the activity of this isozyme and make normal metabolizers resemble poor metabolizers. A subset of the population is a "poor metabolizer" of the enzyme (e.g., debrisoquin hydroxylase) is reduced in a subset of the population. In addition, the long halflife of the parent and active metabolite (at least 20 days) makes it desirable to monitor TCA plasma levels whenever a TCA is going to be co-administered with another drug known to be an inhibitor of P450 2D6.

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clinical trials of PRUDOXIN Cream did not include sufficient numbers of subjects aged 75 or 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 tailored to the patient’s needs and should be reflected in dose selection in elderly patients. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection.

Seeding drugs may cause confusion and oversedation in the elderly; therefore, hospital monitoring is required as soon as possible.

The extent of renal excretion of doxepin has not been determined.

DOSAGE AND ADMINISTRATION

The principles of management of child and adult overdoses are similar. It is strongly recommended that the physician contact the local poison control center for specific pediatric treatment.

Post Marketing Experience

Twenty-six cases of allergic contact dermatitis have been reported in patients using PRUDOXIN Cream, twenty of which were documented by positive patch test to doxepin 5% cream.

OVERDOSAGE

Deaths may occur from overdose with this class of drugs. In children, the potential for abrupt deterioration makes pediatric management of child acute overdosage is similar. It is strongly recommended that the physician contact the local poison control center for specific pediatric treatment.

Pediatric Management: The principles of management of child and adult overdoses are similar. It is strongly recommended that the physician contact the local poison control center for specific pediatric treatment.

Cardiovascular: A maximal limit-lead QRST duration of >0.10 seconds may be the best indication of the severity of the overdose. Intravenous sodium bicarbonate should be used to maintain the serum pH in the range of 7.45 to 7.55. If the pH response is inadequate, hyperventilation may also be used. The presence of hyperventilation and sodium bicarbonate should be done with extreme caution, with frequent pH monitoring. A pH of 7.0 is undesirable. Dystrophic unresponsive to sodium bicarbonate therapy/hyperventilation may respond to lidocaine, bretylium or phenytoin. Type 1A and 1C antiarrhythmics are generally contraindicated (e.g., quinidine, disopyramide, and pro- canidimine).

In rare instances, hemoperfusion may be beneficial in acute refractory cardiovascular instability in patients with acute toxicity. However, hemodialysis, peritoneal dialysis, exchange transfusions, and forced diuresis generally have been reported as ineffective in tricyclic antidepressant poisoning.

CNS: In patients with CNS depression, early intubation is advisable because of the potential for abrupt deterioration. Seizures should be controlled with benzodiazepines, or if ineffective, other anticonvulsants (e.g., phenytoin, phenobarbital, carbamazepine). Physostigmine is not recommended except to treat life-threatening symptoms that have been unresponsive to other therapies, and then only in consultation with a poison control center.

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