Clinical Pharmacology

Introduction

Trientine hydrochloride is a copper chelating agent used for the treatment of Wilson's disease. It is a further development of d-penicillamine. Unlike its predecessor, trientine hydrochloride is not capable of binding cystine and, therefore, it is of no use in cystinuria. In 15 patients with Wilson's disease who were intolerant of penicillamine, trientine hydrochloride capsules USP 250 mg was used when continued treatment with penicillamine was no longer possible because of intolerable or life-threatening side effects.

Unlike penicillamine, trientine hydrochloride capsules USP 250 mg are not recommended in cirrhotics or neutrophilic arthritides. Data on the pharmacokinetics of trientine hydrochloride are not available. Dosage adjustment recommendations are based upon clinical use of the drug (see DOSAGE AND ADMINISTRATION).

Indications and Usage

Trientine hydrochloride capsules USP 250 mg is indicated in the treatment of patients with Wilson's disease who are intolerant of penicillamine. Clinical experience with trientine hydrochloride has also included patients with Wilson's disease who have not been well-characterized at entry points in determining individuals whose disease has not been well-defined. Patients with Wilson's disease must be evaluated and continued treatment with penicillamine cannot be substituted interchangeably. Trientine hydrochloride capsules USP 250 mg should be used when continued treatment with penicillamine is no longer possible because of intolerance or inadequate response to the drug.

Contraindications

Hypersensitivity to this product.

Warnings

Patients with Wilson's disease have a low urinary copper excretion rate and one of the reasons for this is the accumulation of copper in the liver. The body's capability for excreting copper is decreased in patients with Wilson's disease. The mechanism of copper retention in patients with Wilson's disease is unclear. It is thought that the liver lacks the mechanism to excrete free copper into the bile. Hepatocytes may contain excess copper but when their capacity is exceeded copper is released into the blood and is taken up by other tissues.

The most frequent adverse reactions were tremor, rigidity, mutism, and extrapyramidal reaction. The neurological status in the trientine hydrochloride group was unchanged in 7 patients, improved in 4 patients, and remained unchanged in 3 patients. Kayser-Fleischer rings improved significantly in one patient. The neurological status in the trientine hydrochloride group was unchanged in 7 patients, improved in 4 patients, and remained unchanged in 3 patients.

Cholestatic hepatic disease due to copper deposition in the liver is a serious complication. Patients with Wilson's disease who are intolerant of penicillamine should be used to treat the condition in patients who are not capable of receiving d-penicillamine. The efficacy of trientine hydrochloride is limited and alternate dosing regimens have not been well-characterized in determining individual patients whose disease has not been well-defined. Patients with Wilson's disease who are intolerant of penicillamine should be treated with trientine hydrochloride capsules USP 250 mg in patients whose disease has not been well-defined. Patients with Wilson's disease who are intolerant of penicillamine should be treated with trientine hydrochloride capsules USP 250 mg.
regard medical supervision throughout the period of drug administration. Patients particularly women should be closely monitored for evidence of non-deficiency anemia.

PRECAUTIONS

General
There are no reports of hypersensitivity in patients who have been administered trientine hydrochloride for Wilson’s disease. However, there have been reports of selective, bronchial and dermatologic attacks after prolonged environmental exposure in workers

Gastrointestinal
Drug Interactions
Trientine hydrochloride is not indicated for treatment of biliary cirrhosis, but in a new study, it was found that trientine hydrochloride reduced the incidence of biliary cirrhosis, the following adverse reactions were reported: fever, achlorhydria, neutropenia, thrombocytopenia, anemia, pneumonia, rhabdomyolysis. A causal relationship of these reactions to drug therapy could not be reestablished or established.

To report SUSPECTED ADVERSE REACTIONS, contact Novadoz Pharmaceuticals LLC at 1-855-668-2369 or FDA at 1-888-FDA-1088 or www.fda.gov/medwatch.

Information for Patients

Precautions

Drug Interactions
Trientine hydrochloride capsules, USP 250 mg, are capsules with light brown opaque

DOSAGE AND ADMINISTRATION
Dose should be individualized according to the patient’s response and the serum copper levels. The daily dose of trientine hydrochloride capsules USP 250 mg is 500 to 750 mg/day for pediatric patients and 750 to 1250 mg/day for adults given in divided doses two, three or four times daily. This may be increased to a maximum of 2000 mg/day for adults or 1500 mg/day for pediatric patients age 12 or under.

The daily dose of trientine hydrochloride capsules USP 250 mg may be increased only when the clinical response is not adequate or the concentration of free serum copper is persistently above 20 mcg/dL. Optimal long-term maintenance dosage should be determined at 6 to 9 month intervals (see PRECAUTIONS).

Trientine hydrochloride is teratogenic in rats at doses similar to the human dose. Pregnancy Category C

Carcinogenesis, Mutagenesis, Impairment of Fertility

Other reported clinical experience is insufficient to determine differences in response between the elderly and younger patients in general, dose selection should be cautious, usually starting at the low end of the dosage range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapies.

ADVERSE REACTIONS

Clinical experience with trientine hydrochloride has been limited. The following adverse reactions have been reported in clinical studies in patients with Wilson’s disease who were on therapy with trientine hydrochloride (see table below). In addition, the following adverse reactions have been reported in marketed use: dystonia, muscular spasm, rhabdomyolysis, fever, rash, myasthenia gravis. In addition, the following adverse reactions have been reported in marketed use: dystonia, muscular spasm, myasthenia gravis.

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OVERDOSAGE

There is a report of an adult woman who ingested 30 grams of trientine hydrochloride without apparent ill effects. No other data on over dosage are available.

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DOSAGE AND ADMINISTRATION

Systemic evaluation of dose and/or interval between dose has not been done. However, on initial clinical experience, the recommended initial dose of trientine hydrochloride capsules (USP 250 mg) is 500 to 750 mg/day for pediatric patients and 750 to 1250 mg/day for adults given in divided doses two, three or four times daily. This may be increased to a maximum of 2000 mg/day for adults or 1500 mg/day for pediatric patients age 12 or under.

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It is reported that trientine hydrochloride capsules USP 250 mg be taken on an empty stomach, at least one hour before meals or two hours after meals and at least one hour apart from any other drug, food, or milk. The patient should be advised to report any symptom such as fever or skin eruption.

However, iron deficiency may develop, especially in children

Surgical

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