Taj Pharmaceuticals Ltd.

Metamizol Magnesium

CAS No. : 6150-97-6

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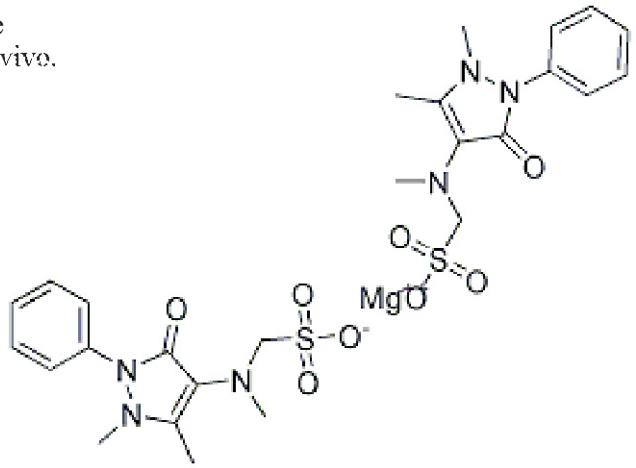
CAS No. 6150-97-6
Molecular Formula: C26H32MgN6O8S2

Effects of metamizol and magnesium sulfate on enzyme activity of glucose 6-phosphate dehydrogenase from human erythrocyte in vitro and rat erythrocyte in vivo.



Chemical data

Formula C13H16N3NaO4S
Mol. mass 311.358 g/mol

Pharmacokinetic data

Bioavailability ?
Metabolism AM404, P Cytochrome P 450, glutation
Half life 1 - 4 hours
Excretion renal

DOSAGE

Recommended dosage

The usual dosage for adults is 20 mg, four times a day. However, the physician may recommend starting at a lower dosage and gradually increasing the dose to reduce the chance of unwanted side effects.

The dosage for children depends on the child's age. Check with the child's physician for the correct dosage.

SIDE EFFECTS

The most common side effects are dizziness, drowsiness, lightheadedness, nausea, nervousness, blurred vision, dry mouth, and weakness. Other side effects may occur.

Major adverse reactions (which occur with much less frequency than the minor adverse reactions) include inhibition of myelopoieses (agranulocytosis, granulocy-topenia, and thrombocytopenia), aplastic anemia, drug fever, a lupuslike syndrome, insulin autoimmune syndrome (which can result in hypoglycemic coma), hepatitis (jaundice may persist for several weeks after discontinuation of the drug), periar-teritis, and hypoprothrombinemia. Nephritis occurs very rarely.

Minor adverse reactions include skin rash, urticaria, nausea, vomiting, epigastric distress, arthralgia, paresthesia, loss of taste, abnormal loss of hair, myalgia, headache, pruritus, drowsiness, neuritis, edema, vertigo, skin pigmentation, jaundice, sialadenopathy, and lymphadenopathy.

It should be noted that about 10% of patients with untreated hyperthyroidism have leukopenia (white-blood-cell count of less than 4,000/mm3), often with relative granulopenia.

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PRECAUTIONS

General

Patients who receive Metamizol Magnesium should be under close surveillance and should be cautioned to report immediately any evidence of illness, particularly sore throat, skin eruptions, fever, headache, or general malaise. In such cases, white-blood-cell and differential counts should be made to determine whether agranulocytosis has developed. Particular care should be exercised with patients who are receiving additional drugs known to cause agranulocytosis.

Laboratory Tests

Because Metamizol Magnesium may cause hypoprothrombinemia and bleeding, prothrombin time should be monitored during therapy with the drug, especially before surgical procedures

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 2 year study, rats were given methimazole at doses of 0.5, 3, and 18 mg/kg/day. These doses were 0.3, 2, and 12 times the 15 mg/day maximum human maintenance dose (when calculated on the basis of surface area). Thyroid hyperplasia, adenoma, and carcinoma developed in rats at the two higher doses.
Pregnancy Categoryused judiciously is an effective drug in hyperthyroidism complicated by pregnancy. In many pregnant women, the thyroid dysfunction diminishes as the pregnancy proceeds; consequently, a reduction in dosage may be possible. In some instances, use of Metamizol Magnesium can be discontinued 2 or 3 weeks before delivery.

INTERACTION

Anticoagulants (oral): The activity of oral anticoagulants may be potentiated by anti-vitamin-K activity attributed to Metamizol Magnesium .blocking agents: Hyperthyroidism may cause an increased clearance of beta ratio. A dose reduction of beta-adrenergic blockers may be needed when a hyperthyroid patient becomes euthyroid. Digitalis glycosides: Serum digitalis levels may be increased when hyperthyroid patients on a stable digitalis glycoside regimen become euthyroid; reduced dosage of digitalis glycosides may be required.Thheophylline: Theophylline clearance may decrease when hyperthyroid patients on a stable theophylline regimen become euthyroid; a reduced dose of theophylline may be needed.

DRUG DESCRIPTION

Metamizol is hydrolyzed in the gastrointestinal tract to the pharmacologically active metabolite 4-methyl-amino-antipyrine (4-MAA), which is transformed by both, oxidation to 4-formyl-amino-antipyrine (4-FAA) and demethylation to 4-amino-antipyrine (4-AA). 4-AA is acetylated to 4-acetyl-amino-antipyrine (4-AcAA). The aim of the present study was to investigate whether cimetidine will alter the pharmacokinetics of the metabolites of metamizol due to cimetidine-induced inhibition of the metabolic transformation of 4-MAA. The study was carried out in 12 patients with duodenal ulcer treated with cimetidine 1,000 mg daily over 20 days. A single oral dose of metamizol 1,500 mg was administered 2 days prior to commencement of cimetidine therapy to all patients. Two further doses of 750 and 1,500 mg of metamizol were given in a randomized order on days 8 and 13 during cimetidine treatment. Blood samples for determination of metamizol metabolites were drown over 48 hours post dose. Drug assays for metamizol metabolites and cimetidine were performed using HPLC methods. The patients were phenotyped for CYP2D6 and acetylation polymorphism. The results revealed that cimetidine interacted with 4-MAA by increasing the systemic availability, prolonging the elimination half-life and decreasing the systemic clearance of 4-MAA, whereas the renal clearances of 4-MAA remained unchanged. Consistent with cimetidine-induced changes in the oxidation of 4-MAA to 4-FAA, as well as in the demethylation of 4-MAA to 4-AA, were the decreased rates of production and the lower maximum concentrations of 4-FAA and 4-AA when metamizol was administered during cimetidine treatment ($p < 0.05$).

No correlation was found between the decrease in the production rates of 4-FAA induced by cimetidine and the hydroxylation abilities of the patients, this suggesting that CYP2D6 is not involved in the metabolism of 4-MAA to 4-FAA. The acetylation of 4-AA to 4-AcAA was not affected by cimetidine. Cimetidine produced an increase not proportional to the dose in the systemic availability only of 4-MAA, whereas the kinetics of the other metabolites changed proportionally to the increasing dose of metamizol.

Metamizol Magnesium is a white, crystalline substance that is freely soluble in water. It differs chemically from the drugs of the thiouracil series primarily because it has a 5- instead of a 6-membered ring. Each tablet contains 5 or 10 mg (43.8 or 87.6 µmol) Metamizol Magnesium , an orally administered antithyroid drug.

Each tablet also contains lactose monohydrate, magnesium stearate, starch (corn), pregelatinized starch and talc.

Antispasmodic drugs have been used to treat stomach cramps. Traditionally, they were used to treat stomach ulcers, but for this purpose they have largely been replaced by the acid inhibiting compoundsa, the H-2 receptor blockers such as cimetidine and ranitidine and the proton pump inhibtors such as omeprazole, lansoprazole and rabetazole.
Most of the drugs used for this purpose as "anti-cholinergics", since they counteract the effects of the neurohormone acetylcholine. Some of these drugs are derived from the plant belladonna, also known as Deadly Nightshade. There is also a group of drugs with similar activity, but not taken from plant sources. The anticholingergics decrease both the movements of the stomach and intestine, and also the secretions of stomach acid and digestive enzymes. They may be used for other purposes including treatment of Parkinson's Disease, and bladder urgency. Because these drugs inhibit secretions, they cause dry mouth and dry eyes because of reduced salivation and tearing. Dicyclomine is an antispasmodic with very lettle effect on secretions. It is used to treat irritable bowel syndrome.

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The Controlled Substances Act (CSA) was enacted into law by the Congress of the United States as Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970.[1] The CSA is the federal U.S. drug policy under which the manufacture, importation, possession, use and distribution of certain substances is regulated. The Act also served as the national implementing legislation for the Single Convention on Narcotic Drugs

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