Dorixina B1,B6,B12

Lysine clonixinate / Vitamins B1, B6, B12

Oral use
Film-coated tablets

Formula
Each film-coated tablet contains Lysine clonixinate 125 mg; Thiamine mononitrate 50 mg; Pyridoxine hydrochloride 30 mg; Cyanocobalamin 50 mcg. Excipients: Mannitol; Povidone K90; Colloidal silicon dioxide hydrophobic; Microcrystalline cellulose; Magnesium stearate; Sodium starch glycolate; Allura red aluminum lake; Sunset yellow aluminum lake; Polyvinyl alcohol; Titanium dioxide; Talc; Polyethylene glycol 3000.

Therapeutic Action
Analgesic, anti-inflammatory.

Indications
Dorixina B1, B6, B12 is indicated for the symptomatic and short-term treatment of musculoskeletal acute inflammatory processes with neuritic component when patients do not respond to treatment with the mono substance.

Pharmacological Action
Lysine clonixinate is a non-steroidal anti-inflammatory drug, with mainly analgesic action. It exerts its effect by inhibiting prostaglandin synthesis. It was recently shown that it acts principally on the enzyme that catalyzes the production of prostaglandins responsible for inflammation (cyclooxygenase-2 or COX-2) with less activity on the enzyme that catalyzes the synthesis of prostaglandins of the gastrointestinal mucosa and the kidneys (cyclooxygenase-1 or COX-1), where these substances have a protective effect. Thiamine (Vitamin B1), Pyridoxine (Vitamin B6) and Cyanocobalamin (Vitamin B12) are water soluble vitamins. Thiamine combines with adenosine triphosphate (ATP) leading to a coenzyme required for carbohydrate metabolism. Pyridoxine is converted in red blood cells into pyridoxal phosphate, acting as coenzyme in various metabolic processes affecting lipid, carbohydrate and protein uptake. It also acts in the conversion of tryptophan to niacin or serotonin, in the fragmentation of glycogen to glucose-1-phosphate, in the synthesis of gamma-aminobutyric acid (GABA) in the CNS and in hem synthesis. Cyanocobalamin acts as coenzyme in various metabolic processes, such as carbohydrate and lipid metabolism and protein synthesis. It is required for development, cell replication, haematopoiesis, nucleoprotein and myelin synthesis, and it is concerned in the metabolism of methionine, folic acid and malonic acid.

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Pharmacokinetics:
Lysine clonixinate is rapidly absorbed reaching its peak plasma level about 40 to 60 minutes following administration. Its bioavailability is of about 56%, with some individual variability. The plasma half-life of Lysine clonixinate in humans is of about 1.75 ± 0.10 hours (mean ± SD). It is excreted in the form of metabolites, principally in the urine (60%). Its concentration in milk is of about 7 to 10% of the plasma concentration. B-vitamins are rapidly absorbed from the gastrointestinal tract, metabolized in the liver and excreted nearly completely in the form of metabolites through the urine, with the exception of vitamin B12 which also shows biliary excretion.

Dosage and Administration
Adults and children over 12 years of age: Unless otherwise prescribed, administer 1 tablet 3 or 4 times per day at regular intervals, according to pain intensity.
Swallow the tablets whole, without chewing them and with abundant liquid.
Maximum daily dosage: 6 tablets.

Contraindications
Known hypersensitivity to Lysine clonixinate or B-vitamins. Active peptic ulcer or gastroduodenal hemorrhage. In patients with a history of bronchospasms, nasal polyps, angioedema or urticaria caused by the administration of acetylsalicylic acid (aspirin) or other non-steroidal anti-inflammatory drugs. Pregnancy. Nursing. Children under 12 years of age.
Advanced renal or hepatic failure. Due to the pyridoxine contents a benefit-risk evaluation should be considered when administering to patients with Parkinson disease.

Warnings
In cases of allergic reactions of skin and/or mucosal tissue or symptoms of peptic ulcer or gastrointestinal hemorrhage discontinue treatment with **Dorixina B1, B6, B12** and contact your physician. Patients with a history of serious gastrointestinal events and other known risk factors associated with peptic ulcer (alcoholism, tobaccoism) are under greater risk. Elderly or weak patients seem to have a decreased tolerance to ulceration or bleeding and therefore report a greater incidence of spontaneous gastrointestinal episodes.
High doses of pyridoxine during large periods (30 days) may develop pyridoxine dependence.

Precautions
Caution should be used when administering to patients with a history of digestive diseases like gastroduodenal peptic ulcer or gastritis and in patients treated with anticoagulants.
It is known that NSAIDs inhibit the synthesis of prostaglandins which have a supportive role in the maintenance of renal perfusion. In patients with impaired renal blood-flow administration of NSAIDs may precipitate overt renal decompensation, usually reversible with the discontinuation of the product. Patients at greatest risk of this reaction are dehydrated patients, patients with congestive heart failure, hepatic cirrhosis, nephrotic syndrome or other overt renal diseases, patients taking diuretics or those who underwent major surgeries with subsequent hypovolemia. In these patients diuresis volume and renal function should to be controlled before initiating therapy.
During treatment with NSAIDs in some cases transaminase plasma levels or other liver parameters may be increased.
Pregnancy: Although preclinical toxicological studies performed with Lysine clonixinate did not show teratogenic effects, there is no sufficient experience available with the administration of **Dorixina B1, B6, B12** to pregnant women. Therefore it should not be administered during pregnancy.
Nursing: As the components of this product are excreted in human milk, as a precautionary measure it should not be administered to breast-feeding women.
Pediatric use: There are no clinical studies available with Lysine clonixinate administered to children under 12 years of age, therefore its use is contraindicated in patients of this age group.
Geriatric use: Like with other anti-inflammatories, it should be administered with caution to elderly patients, as they may have impairment of their cardiac, hepatic or renal function.

Drug Interactions

Other NSAIDs (including acetylsalicylic acid): Increased risk of peptic ulcer and gastroduodenal hemorrhages and of other adverse effects due to their synergistic action.

Oral anticoagulants, ticlopidine, heparin and thrombolytics: Increased risk of hemorrhages. If concomitant administration is unavoidable, close controls of blood coagulation must be performed adjusting the dosage of those medicines which modify coagulation parameters accordingly.

Lithium: Usually NSAIDs increase lithium plasma levels. Closely monitor lithium plasma levels when starting, modifying or discontinuing treatment with **Dorixina B1, B6, B12**.

Methotrexate: Concomitant treatment with methotrexate and NSAIDs may increase hematological toxicity of methotrexate. In these cases, close hematological controls should be performed.

Diuretics: In dehydrated patients, treatment with NSAIDs increases the potential risk of acute renal failure. In cases of concomitant treatment with Lysine clonixinate and diuretics patients must be properly hydrated and their renal function controlled before initiating treatment.

Antihypertensives (for example, beta-adrenergic receptor blocking agents, ACE-inhibitors, vasodilators, diuretics): During concomitant treatment with antihypertensive agents and NSAIDs a decrease in antihypertensive effect has been reported due to the inhibition of vasodilating prostaglandins.

Corticosteroids: Concomitant treatment with corticosteroids and NSAIDs increases the risk of gastrointestinal toxicity including peptic ulcer and hemorrhage.

Hypoglycemic agents: NSAIDs may increase the hypoglycemic effect of these substances as prostaglandins are directly involved in the regulation of glucose metabolism and probably also due to displacement from protein binding in the case of oral hypoglycemic agents.

Probenecid: It may decrease excretion of NSAIDs and increase their plasma levels.

Vitamins B1, B6, B12: Following drugs are pyridoxine antagonists and may cause anemia or peripheral neuritis: Chloramphenicol, cycloserine, hydralazine, corticosteroids, azathioprine, chlorambucil, cyclophosphamide, cyclosporine, mercaptopurine, isoniazid, and penicillamine. Estrogens increase pyridoxine requirements. It should not be coadministered with levodopa as 5 mg of pyridoxine revert its anti-parkinsonian effects. Alcohol intake decreases thiamine absorption. Extended release potassium formulations as well as cholestyramine, colchicine, neomycin and amino-salycilates decrease the absorption of vitamin B12. Ascorbic acid may inactivate vitamin B12.

Adverse Reactions

When administering **Dorixina B1, B6, B12** to sensitive patients, nausea, vomiting, gastritis and somnolence may occur.

Very rarely serious allergic reactions were reported (anaphylaxis) with B-vitamins. These reactions are more frequent during parenteral administration and may include: Cough, difficulty to swallow, pruritus, stiffness of the face, lips and eyelids, sibilance, dyspnea.

Ingestion of the tablets may cause a sensation of abdominal fullness or pyrosis which disappears without the need of treatment discontinuation. Less frequently gastroduodenal ulcer, perforation and occult digestive hemorrhages were reported.

Overdosage

Symptoms of acute overdosage due to NSAIDs are usually limited to lethargy, somnolence, nausea, vomiting, and epigastric pain. Gastrointestinal bleeding may occur. Very rarely hypertension, acute renal failure, respiratory depression and coma may occur.

No cases of overdosage with **Dorixina B1, B6, B12** have still been informed. After a thorough evaluation of the patient, considering the time lapsed from administration, the amount of drugs taken and once having discarded any contraindication regarding certain procedures, the physician will decide upon carrying out the general rescue treatment: Gastric evacuation (vomiting or gastric lavage), close clinical control (specially gastroduodenal and renal function) and symptomatic supportive care. No specific antidotes have yet been described.

How Supplied

Dorixina B1, B6, B12 film-coated tablets: Packages containing 20 film-coated tablets

◯ Red, cylindrical film-coated tablets

Swallow the tablets whole, without chewing them and with abundant liquid.

Dispensed under prescription. Made in Argentina.

Medicinal Product.
Keep out of the reach of children.
Keep in a dry place at temperature below 30°C.

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