MEFENAMIC acid

STANGESIC®

500 mg Tablet
Non-Steroidal Anti-Inflammatory Drug (NSAID)

Rx

FORMULATION:
Each film-coated tablet contains:
Mefenamic acid, BP ..... 500 mg

DESCRIPTION:
Mefenamic acid (Stangesic®) 500 mg tablet is a light yellow, oval, biconvex, film-coated tablet, bisected on one side, plain on the other.

Stangesic® is the brand of Mefenamic acid which has demonstrated analgesic, antipyretic and anti-inflammatory effects. In tests of analgesia, it displays a central as well as a peripheral action. These actions appear to be via inhibition of prostaglandin-forming cyclooxygenase.

PHARMACODYNAMICS AND PHARMACOKINETICS:
Mefenamic acid is a non-steroidal agent with demonstrated anti-inflammatory, analgesic and antipyretic activity in laboratory animals. Mefenamic acid was found to inhibit prostaglandin synthesis and to compete for binding at the prostaglandin receptor sites in animal models.

Mefenamic acid is rapidly absorbed from the gastrointestinal tract. Following administration of a one gram oral dose to adults, peak plasma levels of 10 µg/mL occur in 1 to 4 hours, with half-life of 2 hours. Plasma levels are proportional to dose, following multiple doses, with no drug accumulation. One gram of mefenamic acid administered four times daily produces peak blood levels of 20 µg/mL by the second day of administration.

Mefenamic acid is extensively bound to plasma proteins.

Mefenamic acid metabolism is predominantly mediated via cytochrome P450 CYP2C9 in the liver. Patients who are known or suspected to be poor CYP2C9 metabolizers based on previous history/experience with other CYP2C9 substrates should be administered mefenamic acid with caution as they may have abnormally high plasma levels due to reduced metabolic clearance.

Following a single oral dose, 52-67% of the dose was recovered from the urine as unchanged drug or one of two metabolites. Assay of stools over 3 days accounted for 20-25% of the dose, chiefly as unconjugated metabolite II.

INDICATIONS:
Relief of mild to moderate pain arising from rheumatoid arthritis (including Still's disease), soft tissue injuries, other painful musculoskeletal conditions, headache, dental pain, post-operative pain and dysmenorrhea.

DOSAGE AND ADMINISTRATION:
Unless otherwise prescribed by the physician, the usual adult oral dose of Mefenamic acid is as follows:

Adults and Children > 12 years: 1 tablet as initial dose followed by 1/2 tablet every 8 hours as needed (not to be given > 7 days).
Preferably administered with food.

WARNINGS AND PRECAUTIONS:
Treatment with mefenamic acid should not be continued > 7 days. Mefenamic acid is not recommended for use in children, pregnant women and nursing mothers. It should be used with caution in patients with impaired renal and liver function. Concomitant therapy with plasma-protein-binding drugs may require modification in dosage. If anticoagulants are being administered, the dose may need to be reduced. If skin rash, diarrhea or other significant gastrointestinal discomfort occurs, Mefenamic acid (Stangesic®) should be discontinued and consultation with physician is advised.

CONTRAINDICATIONS:
Mefenamic acid (Stangesic®) is contraindicated in patients with known hypersensitivity to mefenamic acid, in patients with active peptic ulcer or inflammatory bowel disease, and in patients with hepatic and renal impairment. Cross-sensitivity with aspirin and other NSAIDs may occur and elicit allergic symptoms, e.g., bronchoconstriction.

ABSOLUTE CONTRAINDICATIONS:
Not to be given to those patients who have history of: Stroke, Cerebrovascular accident (CVA), Heart attack, Myocardial infarction (MI), Coronary artery bypass graft (CABG), Uncontrolled hypertension and Congestive heart failure (CHF), NYHA II-IV.

PREGNANCY AND LACTATION:
Pregnancy
Since there are no adequate and well-controlled studies in pregnant women, this drug should be used only if the potential benefits to the mother justify the possible risk to the fetus. It is not known if mefenamic acid or its metabolites cross the placenta. However, because of the effects of drugs in this class (i.e., inhibitors of prostaglandin synthesis) on the fetal cardiovascular system (e.g., premature closure of the ductus arteriosus), the use of mefenamic acid in pregnant women is not recommended. Mefenamic acid inhibits prostaglandin synthesis which may result in prolongation of pregnancy and interference with labor when administered late in the pregnancy. Women on mefenamic acid therapy should consult their physician if they decide to become pregnant.
Inhibition of prostaglandin synthesis might adversely affect pregnancy. Data from epidemiological studies suggest an increased risk of spontaneous abortion after use of prostaglandin synthesis inhibitors has been shown to result in increased pre- and post-implantation loss.

Lactation
Trace amounts of mefenamic acid may be present in breast milk and transmitted to the nursing infant. Therefore, mefenamic acid should not be taken by nursing mothers.

DRUG INTERACTIONS:
Acetylsalicylic acid: Mefenamic acid interferes with the anti-platelet effect of low-dose aspirin, and thus may interfere with aspirin's prophylactic treatment of cardiovascular disease.

Anticoagulants: Mefenamic acid has been shown to displace warfarin from protein binding sites, and may enhance the response to oral anticoagulants. Therefore, concurrent administration of mefenamic acid with oral anticoagulant drugs requires frequent prothrombin time monitoring.

Anti-hypertensives including diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II antagonists (AIIA) and beta-blockers: NSAIDs can reduce the efficacy of diuretics and other antihypertensive drugs, including ACE inhibitors, AIIA and beta blockers.

In patients with impaired renal function (e.g. dehydrated patients or elderly patients with compromised renal function), the co-administration of an ACE inhibitor or an AIIA and/or diuretics with a cyclo-oxygenase inhibitor can increase the deterioration of the renal function, including the possibility of acute renal failure, which is usually reversible. The occurence of these interactions should be considered in patients taking mefenamic acid with an ACE inhibitors or an AIIA and/or diuretics.

Therefore, the concomitant administration of these drugs should be done with caution, especially in elderly patients. Patients should be adequately hydrated and the need to monitor the renal function should be assessed in the beginning of the concomitant treatment and periodically thereafter.

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding.

Cyclosporine: Because of their effect on renal prostaglandins, NSAIDs such as mefenamic acid may increase the risk of nephrotoxicity with cyclosporine.

Hypoglycemic agents: There have been reports of changes in the effects of oral hypoglycemic agents in the presence of NSAIDs. Therefore, mefenamic acid should be administered with caution in patients receiving insulin or oral hypoglycemic agents.

Lithium: Mefenamic acid has produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. Thus, when mefenamic acid and lithium are administered concurrently, patients should be observed carefully for signs of lithium toxicity.

Methotrexate: Caution is advised when methotrexate is administered concurrently with NSAIDs, including mefenamic acid because NSAID administration may result in increased plasma levels of methotrexate, especially in patients receiving high doses of methotrexate.

Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

ADVERSE EFFECTS:

The most common side effects involve the gastrointestinal system in the form of dyspepsia, upper GIT discomfort, diarrhea or constipation and abdominal pain. Other reactions noted less frequently include transient abnormalities of hepatic or renal function, CNS effects including headache, drowsiness, nervousness and visual disturbances, skin rashes and urticaria. Allergic glomerulonephritis known to be associated with prostaglandin inhibitors, and reversible non-oliguric renal failure has been reported. A positive test for bile in the urine of patients receiving mefenamic acid is not due to the presence of bile, but due to the presence of the drug and its metabolites in the urine. Hematological effects noted with long-term treatment include hemolytic anemia, agranulocytosis, pancytopenia, thrombocytopenia, or thrombocytopenic purpura and bone marrow aplasia.

OVERDOSE:

Following accidental overdosage, the stomach should be emptied immediately by inducing emesis or by the gastric lavage, followed by administration of activated charcoal. Vital functions should be monitored and supported. Hemodialysis is of little value since mefenamic acid and its metabolites are firmly bound to plasma proteins.

Seizures, acute renal failure, coma, confusional state, vertigo, and hallucination have been reported with mefenamic acid overdoses.

Overdose has led to fatalities.

STORAGE CONDITION:

Store at temperatures not exceeding 30°C.

KEEP OUT OF REACH OF CHILDREN.

AVAILABILITY:

Alu/PVC Blister Pack of 10's (Box of 40's and 100's)

CAUTION:

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

ADR REPORTING:

For suspected adverse drug reaction, report to the FDA: **www.fda.gov.ph**

Patient should seek medical attention immediately at the first sign of any adverse drug reaction.

REGISTRATION NUMBER:

DRP-7761

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Stangesic® is a registered mark of **GX INTERNATIONAL, INC.**

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