Mefenamic Acid

Revalan®

500 mg Tablet
Non-Steroidal Anti-inflammatory

Trusted Quality Healthcare

FORMULATION
Each scored film-coated tablet contains:
Mefenamic Acid ..... 500 mg

PRODUCT DESCRIPTION
Revalan is an elliptically-shaped, light yellow-colored tablet, scored on one side and plain on the other side.

PHARMACODYNAMICS
Mefenamic acid has anti-inflammatory, analgesic (pain-reducing), and antipyretic (fever-reducing) activities. It inhibits cyclooxygenase (COX)-1 and COX-2 isoenzymes which in turn inhibits synthesis and release of a group of chemicals called prostaglandins. Prostaglandins are involved in the way we feel pain and the development of fever and inflammation.
Unlike most other NSAIDs, mefenamic acid also appears to compete with prostaglandins for binding at the prostaglandin receptor site and thus potentially affect prostaglandins that have already been formed. Mefenamic acidis antipyretic and analgesic properties are due to its central (action on the brain) and peripheral (action at the site of tissue injury or inflammation) mechanisms.

PHARMACOKINETICS
Mefenamic acid is rapidly absorbed after oral administration. Peak plasma concentrations occur about 2 to 4 hours after ingestion. The plasma elimination half-life is approximately two hours. Mefenamic acid is extensively bound to plasma proteins. Over 50% of a dose is excreted in the urine as unchanged drug or conjugates of mefenamic acid and its metabolites. Small amounts have been detected in breast milk.

INDICATIONS
- For symptomatic relief of mild to moderate pain including headache, dental pain, post-operative and postpartum pain, primary dysmenorrhea, and menorrhagia.
- For symptomatic relief of musculoskeletal and joint disorders including osteoarthritis and rheumatoid arthritis.

DOSAGE AND ADMINISTRATION
Like other NSAIDs, the lowest effective dose of mefenamic acid should be used for the shortest possible time. Orally, preferably with food.

Adults and Adolescents older than 14 years: 1 tablet every 8 hours as needed or as directed by a doctor
For the relief of dysmenorrhea and premenstrual syndrome (PMS): 1 tablet every 8 hours while symptoms persist ("period pains" and other associated symptoms) or as directed by a doctor.

CONTRAINDICATIONS

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
- Congestive heart failure (CHF) NYHA II-IV

- Patients with history of hypersensitivity to aspirin or any other NSAID
- Patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs.
- Patients with active ulceration or chronic inflammation of either the upper or lower gastrointestinal tract.
- Patients with preexisting renal disease.

WARNINGS
Gastrointestinal Warning: NSAIDs can cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.

Cardiovascular Effects
Cardiovascular Thrombotic Events
Clinical trials using COX-2 selective and nonselective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction, and stroke, which can be fatal. Patients with known CV disease or risk factors for CV disease may be at greater risk. To minimize the potential risk for an adverse CV event in patients treated with an NSAID, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should be alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed on the signs and/or symptoms of serious CV events and the steps to take if they occur.

Hypertension
NSAIDs can lead to the onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. NSAIDs, including mefenamic acid, should be used with caution in patients with hypertension. Blood pressure should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.

Congestive Heart Failure and Edema
Fluid retention and edema have been observed in some patients taking NSAIDs. Mefenamic acid should be used with caution in patients with fluid retention or heart failure.

Renal effects
Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and Angiotensin Converting Enzyme (ACE) inhibitors, and the elderly.

Advanced Renal Disease
There are no controlled studies on the use of mefenamic acid in patients with advanced renal disease; therefore, treatment with mefenamic acid is not recommended in these patients.

Anaphylactoid Reactions
Anaphylactoid reactions may occur in patients without known prior exposure to NSAIDs. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs. Emergency help should be sought in cases where an anaphylactoid reaction occurs.

Skin reactions
As with other NSAIDs, mefenamic acid, can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

PRECAUTIONS
Use with caution in patients with cardiac, liver or kidney disease. Dose adjustment like using the lowest effective dose and monitoring kidney and liver functions should be instituted. Do not exceed the recommended dose or duration of treatment. Long term continuous use may increase the risk of heart attack or stroke.

Hepatic Effects
Patients with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with mefenamic acid. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash), mefenamic acid should be discontinued.

Hematological Effects
Anemia is sometimes seen in patients receiving NSAIDs including mefenamic acid. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect on erythropoiesis.

High Risk Group
Geriatric Use As with other NSAIDs, caution should be exercised in treating the elderly (65 years and older).

INTERACTIONS WITH OTHER MEDICATIONS
NSAIDs such as mefenamic acid have the following interactions:

CONCOMITANT DRUG EFFECT	
ACE Inhibitors	• NSAIDs may diminish the antihypertensive effect of ACE-inhibitors
Adrenergic Neuron Blockers	• NSAIDs antagonize the hypotensive effect of adrenergic neuron blockers
Alpha-blockers	• NSAIDs antagonize the hypotensive effect of alpha-blockers
Angiotensin-II Receptor Antagonists	• NSAIDs antagonize the hypotensive effect of angiotensin-II receptor antagonists and increase the risk of renal impairment
Antacids	• Increase in the maximum plasma concentration (C_{max}) and area under the curve (AUC) of mefenamic acid after ingestion of magnesium hydroxide
Antidepressants, SSRIs	• Increased risk of bleeding
Aspirin	• Avoid concomitant use with NSAIDs (increased adverse effects)
Baclofen	• NSAIDs may reduce excretion of baclofen (increased risk of toxicity)
Beta-blockers	• NSAIDs antagonize the hypotensive effect of beta-blockers
Calcium-channel blockers	• NSAIDs antagonize the hypotensive effect of calcium channel blockers
Cardiac glycosides	• NSAIDs may increase plasma concentration of cardiac glycosides
Cyclosporine	• Increased risk of nephrotoxicity
Clonidine	• NSAIDs antagonize the hypotensive effect of clonidine
Clopidogrel	• Increased risk of bleeding
Corticosteroids	• Increased risk of gastrointestinal bleeding and ulceration
Coumarin	• NSAIDs may enhance the anticoagulant effect of coumarins
Diazoxide	• NSAIDs antagonize the hypotensive effect of diazoxide
Diuretics	• Increased risk of nephrotoxicity and antagonism of diuretic effect
Diuretics, Potassium-sparing and aldosterone antagonist	• Possible increased risk of hyperkalemia
Drospirenone	• Risk of hyperkalemia (monitor serum potassium during first cycle)
Heparin	• Possible increased risk of bleeding
Hydralazine	• NSAIDs antagonize the hypotensive effect of hydralazine
Ketorolac	• Avoid concomitant use with ketorolac (increased side effects and hemorrhage)
Lithium	• NSAIDs may reduce the excretion of lithium (increased risk of toxicity)
Methotrexate	• NSAIDs may reduce the excretion of methotrexate (increased risk of toxicity)
Methyldopa	• NSAIDs antagonize the hypotensive effect of methyldopa
Nitroprusside	• NSAIDs antagonize the hypotensive effect of nitroprusside
NSAIDs	• Avoid concomitant use of other NSAIDs (increased side effects)
Penicillamine	• Possible increased risk of nephrotoxicity
Pentoxifylline (oxpentifylline)	• Possible increased risk of bleeding
Phenytoin	• NSAIDs may enhance the effects of phenytoin
Quinolones	• Possible increased risk of convulsions
Sibutramine	• Increased risk of bleeding
Sulfonylureas	• NSAIDs may enhance effects of sulfonylureas
Tacrolimus	• Possible increased risk of nephrotoxicity
Venlafaxine	• Increased risk of bleeding
Zidovudine	• Increased risk of hematologic toxicity

PREGNANCY AND LACTATION

Pregnancy
Pregnancy Category C.
Reproductive studies conducted in rats and rabbits have not demonstrated evidence of developmental abnormalities. However, animal reproduction studies are not always predictive of human response. There are no adequate and well-controlled studies in pregnant women.
Avoid mefenamic acid use during pregnancy (particularly late pregnancy) because of the known effects of NSAIDs on the fetal cardiovascular system (closure of ductus arteriosus).

Labor and Delivery
The effects of mefenamic acid on labor and delivery are unknown.

Breastfeeding Mothers
Trace amounts of mefenamic acid may be present in breast milk. Because of the potential for serious adverse reactions from mefenamic acid in breastfeeding infants, a decision should be made whether to discontinue breastfeeding or to discontinue the drug, taking into account the importance of the drug to the mother.

UNDESIRABLE EFFECTS
Frequently reported adverse events:
Gastrointestinal: abdominal pain, constipation, diarrhea, dyspepsia, flatulence, gross bleeding/perforation, heartburn, nausea, GI ulcers (gastric/duodenal), peptic ulcer, vomiting
Hemic and lymphatic: anemia, increased bleeding time
Hepatic: elevated liver enzymes
Nervous: dizziness, headache
Renal: abnormal renal function, edema
Skin and appendages: pruritus, rash
Others: tinnitus
Occasionally reported adverse events:
Body as a whole: fever, infection, sepsis
Cardiovascular: congestive heart failure, hypertension, tachycardia, syncope
Digestive: dry mouth, esophagitis, gastric/peptic ulcers, gastritis, gastrointestinal bleeding, glossitis, hematemesis, hepatitis, jaundice
Hemic and lymphatic: ecchymosis, eosinophilia, leucopenia, melena, purpura, rectal bleeding, stomatitis, thrombocytopenia
Metabolic and nutritional: weight changes
Nervous: asthenia, anxiety, confusion, depression, dream abnormalities, drowsiness, insomnia, malaise, nervousness, paresthesia, somnolence, tremors, vertigo
Renal: cystitis, dysuria, hematuria, interstitial nephritis, oliguria/polyuria, proteinuria, renal failure
Respiratory: asthma, dyspnea
Skin and appendages: alopecia, photosensitivity, pruritus, sweat
Special senses: blurred vision
Rarely reported adverse events:
Body as a whole: anaphylactoid reactions, appetite changes, death
Cardiovascular: arrhythmia, hypotension, myocardial infarction, palpitations, vasculitis
Digestive: eructation, liver failure, pancreatitis
Hemic and lymphatic: agranulocytosis, hemolytic anemia, aplastic anemia, lymphadenopathy, pancytopenia
Metabolic and nutritional: hyperglycemia
Nervous: convulsions, coma, hallucinations, meningitis
Respiratory: respiratory depression, pneumonia
Skin and appendages: angioedema, erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrosis, urticaria
Special senses: conjunctivitis, hearing impairment

OVERDOSE AND TREATMENT
Coma and tonic-clonic seizures have been reported in a 13-year old girl after ingestion of 5 - 10 g of mefenamic acid. This was resolved after treatment with intravenous diazepam. In humans who reportedly ingested 1.5 - 50 g of mefenamic acid and have plasma drug concentrations ranging from 11-211 g/mL, tonic-clonic seizures, muscle twitching, vomiting, and diarrhea were reported.

In the event of overdose, the stomach should be emptied immediately by inducing emesis or by gastric lavage followed by administration of activated charcoal. Since mefenamic acid is highly bound to plasma proteins, forced diuresis, alkalinization of urine, or hemodialysis are probably of no value in enhancing elimination of the drug.

STORAGE CONDITION
Store at temperatures not exceeding 30ºC

AVAILABILITY
Box of 100 Tablets in Flex Foil

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

Manufactured by:
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