MEFENAMIC ACID- mefenamic acid capsule
Advanced Rx Pharmacy of Tennessee, LLC

Mefenamic Acid 250mg Capsules

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

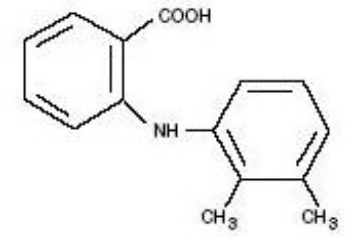
Cardiovascular Thrombotic Events

Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use (see WARNINGS).
Mefenamic acid is contraindicated in the setting of coronary artery bypass graft (CABG) surgery (see CONTRAINDICATIONS, WARNINGS).

Gastrointestinal Bleeding, Ulceration, and Perforation

NSAIDs cause an increased risk of serious gastrointestinal (GI) 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 and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events (see WARNINGS).

Mefenamic Acid Capsules are a member of the fenamate group of nonsteroidal anti-inflammatory drugs (NSAIDs). Each Size '1' Yellow-Yellow capsule, with 'ML' imprinted on the cap & '250' imprinted on the body, contains 250 mg of mefenamic acid for oral administration. Mefenamic acid is a white to greyish-white, odorless, microcrystalline powder with a melting point of 230° to 231°C and water solubility of 0.004% at pH 7.1. The chemical name is N-2,3-xylylanthranilic acid. The molecular weight is 241.29. Its molecular formula is C 15H 15NO 2 and the structural formula of mefenamic acid is:



Each capsule also contains lactose monohydrate. The capsule shell contains D&C yellow No. 10; FD&C blue No. 1; FD&C red No. 3; FD&C yellow No. 6; gelatin, sodium lauryl sulfate, titanium dioxide, black iron oxide, propylene glycol & shellac.

Mechanism of Action

Mefenamic acid has analgesic, anti-inflammatory, and antipyretic properties.

The mechanism of action of mefenamic acid, like that of other NSAIDs, is not completely understood but involves inhibition of cyclooxygenase (COX-1 and COX-2).

Mefenamic acid is a potent inhibitor of prostaglandin synthesis in vitro. Mefenamic acid concentrations reached during therapy have produced in vivo effects. Prostaglandins sensitize afferent nerves and potentiate the action of bradykinin in inducing pain in animal models. Prostaglandins are mediators of inflammation. Because mefenamic acid is an inhibitor of prostaglandin synthesis, its mode of action may be due to a decrease of prostaglandins in peripheral tissues.

Pharmacokinetics

Absorption

Mefenamic acid is rapidly absorbed after oral administration. In two 500-mg single oral dose studies, the mean extent of absorption was 30.5 mcg/hr/mL (17% CV). The bioavailability of the capsule relative to an IV dose or an oral solution has not been studied.

Following a single 1-gram oral dose, mean peak plasma levels ranging from 10 to 20 mcg/mL have been reported. Peak plasma levels are attained in 2 to 4 hours and the elimination half-life approximates 2 hours. Following multiple doses, plasma levels are proportional to dose with no evidence of drug accumulation. In a multiple dose trial of normal adult subjects (n= 6) receiving 1-gram doses of mefenamic acid four times daily, steady-state concentrations of 20 mcg/mL were reached on the second day of administration, consistent with the short half-life.

The effect of food on the rate and extent of absorption of mefenamic acid has not been studied. Concomitant ingestion of antacids containing magnesium hydroxide has been shown to significantly increase the rate and extent of mefenamic acid absorption (see PRECAUTIONS; DRUG INTERACTIONS).

Distribution

Mefenamic acid has been reported as being greater than 90% bound to albumin. The relationship of unbound fraction to drug concentration has not been studied. The apparent volume of distribution (Vzss/F) estimated following a 500-mg oral dose of mefenamic acid was 1.06 L/kg.

Based on its physical and chemical properties, mefenamic acid is expected to be excreted in human breast milk (see PRECAUTIONS; NURSING MOTHERS).

Elimination

Metabolism

Mefenamic acid is metabolized by cytochrome P450 enzyme CYP2C9 to 3-hydroxymethyl mefenamic acid (Metabolite I). Further oxidation to a 3-carboxymefenamic acid (Metabolite II) may occur. The activity of these metabolites has not been studied. The metabolites may undergo glucuronidation and mefenamic acid is also glucuronidated directly. A peak plasma level approximating 20 mcg/mL was observed at 3 hours for the hydroxy metabolite and its glucuronide (n= 6) after a single 1-gram dose. Similarly, a peak plasma level of 8 mcg/mL was observed at 6 to 8 hours for the carboxy metabolite and its glucuronide.

Excretion

Approximately fifty-two percent of a mefenamic acid dose is excreted into the urine primarily as glucuronides of mefenamic acid (6%), 3-hydroxymefenamic acid (25%) and

3 carboxymefenamic acid (21%). The fecal route of elimination accounts for up to 20% of the dose, mainly in the form of unconjugated 3-carboxymefenamic acid.

The elimination half-life of mefenamic acid is approximately two hours. Half-lives of metabolites I and II have not been precisely reported, but appear to be longer than the parent compound. The metabolites may accumulate in patients with renal or hepatic failure. The mefenamic acid glucuronide may bind irreversibly to plasma proteins. Because both renal and hepatic excretions are significant pathways of elimination, dosage adjustments in patients with renal or hepatic dysfunction may be necessary. Mefenamic acid should not be administered to patients with pre-existing renal disease or in patients with significantly impaired renal function (see WARNINGS; RENAL TOXICITY AND HYPERKALEMIA) .

TABLE 1. Pharmacokinetic Parameter Estimates for Mefenamic Acid

PK Parameters	Normal Healthy Adults (18 to 45 yr)	
	Value	CV
T max (hr)	2	66
Oral clearance (L/hr)	21.13	38
Apparent volume of distribution; Vz/F (L/kg)	1.06	60
Half-life; t ½ (hrs)	2 to 4	N/A

Special Populations

Pediatric: Mefenamic acid has not been adequately investigated in pediatric patients less than 14 years of age. A study in 17 preterm infants administered 2 mg/kg indicated that the half-life was about five times as long as adults, consistent with the low activity of metabolic enzymes in newborn infants. The mean C max in this study was 4 mcg/mL (range 2.9 to 6.1). The mean time to maximum concentration (T max) was 8 hours (range 2 to 18 hours).

Race: Pharmacokinetic differences due to race have not been identified.

Hepatic Impairment: Mefenamic acid pharmacokinetics have not been studied in patients with hepatic dysfunction. As hepatic metabolism is a significant pathway of mefenamic acid elimination, patients with acute and chronic hepatic disease may require reduced doses of mefenamic acid compared to patients with normal hepatic function (see WARNINGS; HEPATOTOXICITY).

Renal Impairment: Mefenamic acid pharmacokinetics have not been investigated in subjects with renal insufficiency. Given that mefenamic acid, its metabolites and conjugates are primarily excreted by the kidneys, the potential exists for mefenamic acid metabolites to accumulate. Mefenamic acid should not be administered to patients with pre-existing renal disease or in patients with significantly impaired renal function (see WARNINGS; RENAL TOXICITY AND HYPERKALEMIA).

Drug Interaction Studies

Aspirin: When NSAIDs were administered with aspirin, the protein binding of NSAIDs were reduced, although the clearance of free NSAID was not altered. The clinical significance of this interaction is not known. See Table 2 for clinically significant drug interactions of NSAIDs with aspirin (see PRECAUTIONS; DRUG INTERACTIONS) .

Clinical Studies

In controlled, double-blind, clinical trials, mefenamic acid was evaluated for the treatment of primary spasmodic dysmenorrhea. The parameters used in determining efficacy included pain assessment by both patient and investigator; the need for concurrent analgesic medication; and evaluation of change in frequency and severity of symptoms characteristic of spasmodic dysmenorrhea. Patients received either mefenamic acid, 500 mg (2 capsules) as an initial dose of 250 mg every 6 hours, or placebo at onset of bleeding or of pain, whichever began first. After three menstrual cycles, patients were crossed over to the alternate treatment for an additional three cycles. Mefenamic acid was significantly superior to placebo in all parameters, and both treatments (drug and placebo) were equally tolerated.

Carefully consider the potential benefits and risks of mefenamic acid and other treatment options before deciding to use mefenamic acid. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see WARNINGS; GASTROINTESTINAL BLEEDING, ULCERATION, AND PERFORATION).

Mefenamic acid is indicated:

- For relief of mild to moderate pain in patients ≥ 14 years of age, when therapy will not exceed one week (7 days).
- For treatment of primary dysmenorrhea.

Mefenamic acid is contraindicated in the following patients:

Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to mefenamic acid or any components of the drug product (see WARNINGS; ANAPHYLACTIC REACTIONS, SERIOUS SKIN REACTIONS) .
History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported in such patients (see WARNINGS; ANAPHYLACTIC REACTION, EXACERBATION OF ASTHMA RELATED TO ASPIRIN SENSITIVITY) .
In the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS; CARDIOVASCULAR THROMBOTIC EVENTS) .

Cardiovascular Thrombotic Events

Clinical trials of several COX-2 selective and nonselective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, including myocardial infarction (MI) and stroke, which can be fatal. Based on available data, it is unclear that the risk for CV thrombotic events is similar for all NSAIDs. The relative increase in serious CV thrombotic events over baseline conferred by NSAID use appears to be similar in those with and without known CV disease or risk factors for CV disease. However, patients with known CV disease or risk factors had a higher absolute incidence of excess serious CV thrombotic events, due to their increased baseline rate. Some observational studies found that this increased risk of serious CV thrombotic events began as early as the first weeks of treatment. The increase in CV thrombotic risk has been observed most consistently at higher doses.

To minimize the potential risk for an adverse CV event in NSAID-treated patients, use the lowest effective dose for the shortest duration possible. Physicians and patients should remain alert for the development of such events throughout the entire treatment course, even in the absence of previous CV symptoms. Patients should be informed

about the symptoms of serious CV events and the steps to take if they occur.

There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use. The concurrent use of aspirin and an NSAID, such as mefenamic acid, increases the risk of serious gastrointestinal (GI) events (see WARNINGS; Gastrointestinal Bleeding, Ulceration, and Perforation).

Status Post Coronary Artery Bypass Graft (CABG) Surgery

Two large, controlled, clinical trials of a COX-2 selective NSAID for the treatment of pain in the first 10 to 14 days following CABG surgery found an increased incidence of myocardial infarction and stroke. NSAIDs are contraindicated in the setting of CABG (see CONTRAINDICATIONS).

Post-MI Patients

Observational studies conducted in the Danish National Registry have demonstrated that patients treated with NSAIDs in the post-MI period were at increased risk of reinfarction, CV-related death, and all-cause mortality beginning in the first week of treatment. In this same cohort, the incidence of death in the first year post-MI was 20 per 100 person years in NSAID-treated patients compared to 12 per 100 person years in non-NSAID exposed patients. Although the absolute rate of death declined somewhat after the first year post-MI, the increased relative risk of death in NSAID users persisted over at least the next four years of follow-up.

Avoid the use of mefenamic acid in patients with a recent MI unless the benefits are expected to outweigh the risk of recurrent CV thrombotic events. If mefenamic acid is used in patients with a recent MI, monitor patients for signs of cardiac ischemia.

Gastrointestinal Bleeding, Ulceration, and Perforation

NSAIDs, including mefenamic acid, cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the esophagus, stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Only one in five patients who develop a serious upper GI adverse event on NSAID therapy is symptomatic. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3 to 6 months, and in about 2 to 4% of patients treated for one year. However, even short-term NSAID therapy is not without risk.

Risk Factors for GI Bleeding, Ulceration, and Perforation

Patients with a prior history of peptic ulcer disease and/or GI bleeding who used NSAIDs had a greater than 10-fold increased risk for developing a GI bleed compared to patients without these risk factors. Other factors that increase the risk for GI bleeding in patients treated with NSAIDs include longer duration of NSAID therapy, concomitant use of oral corticosteroids, aspirin, anticoagulants, or selective serotonin reuptake inhibitors (SSRIs); smoking, use of alcohol, older age, and poor general health status. Most postmarketing reports of fatal GI events occurred in elderly or debilitated patients. Additionally, patients with advanced liver disease and/or coagulopathy are at increased risk for GI bleeding.

Strategies to Minimize the GI Risks in NSAID-treated patients:

Use the lowest effective dosage for the shortest possible duration.
Avoid administration of more than one NSAID at a time.
Avoid use in patients at higher risk unless benefits are expected to outweigh the increased risk of bleeding. For such patients, as well as those with active GI bleeding, consider alternate therapies other than NSAIDs.
Remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy.
If a serious GI adverse event is suspected, promptly initiate evaluation and treatment, and discontinue mefenamic acid until a serious GI adverse event is ruled out.
In the setting of concomitant use of low-dose aspirin for cardiac prophylaxis, monitor patients more closely for evidence of GI bleeding (see PRECAUTIONS ; DRUG INTERACTIONS).

Hepatotoxicity

Elevations of ALT or AST (three or more times the upper limit of normal [ULN]) have been reported in approximately 1% of NSAID-treated patients in clinical trials. In addition, rare, sometimes fatal, cases of severe hepatic injury, including fulminant hepatitis, liver necrosis, and hepatic failure have been reported.

Elevations of ALT or AST (less than three times ULN) may occur in up to 15% of patients treated with NSAIDs including mefenamic acid.

Inform patients of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, diarrhea, pruritus, jaundice, right upper quadrant tenderness, and "flu-like" symptoms). If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), discontinue mefenamic acid immediately, and perform a clinical evaluation of the patient.

Hypertension

NSAIDs, including mefenamic acid, can lead to new onset of hypertension or worsening of pre existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking angiotensin converting enzyme (ACE) inhibitors, thiazides diuretics, or loop diuretics may have impaired response to these therapies when taking NSAIDs (see PRECAUTIONS; DRUG INTERACTIONS).

Monitor blood pressure (BP) during the initiation of NSAID treatment and throughout the course of therapy.

Heart Failure and Edema

The Coxib and traditional NSAID Trialists' Collaboration meta-analysis of randomized controlled trials demonstrated an approximately two-fold increase in hospitalizations for heart failure in COX-2 selective-treated patients and nonselective NSAID-treated patients compared to placebo-treated patients. In a Danish National Registry study of patients with heart failure, NSAID use increased the risk of MI, hospitalization for heart failure, and death.

Additionally, fluid retention and edema have been observed in some patients treated with NSAIDs. Use of mefenamic acid may blunt the CV effects of several therapeutic agents used to treat these medical conditions (e.g., diuretics, ACE inhibitors, or angiotensin receptor blockers [ARBs]) (see PRECAUTIONS; DRUG INTERACTIONS).

Avoid the use of mefenamic acid in patients with severe heart failure unless the benefits

are expected to outweigh the risk of worsening heart failure. If mefenamic acid is used in patients with severe heart failure, monitor patients for signs of worsening heart failure.

Renal Toxicity and Hyperkalemia

Renal Toxicity

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, dehydration, hypovolemia, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors or ARBs, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.

No information is available from controlled clinical studies regarding the use of mefenamic acid in patients with advanced renal disease. The renal effects of mefenamic acid may hasten the progression of renal dysfunction in patients with pre-existing renal disease.

Correct volume status in dehydrated or hypovolemic patients prior to initiating mefenamic acid. Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia during use of mefenamic acid (see PRECAUTIONS; DRUG INTERACTIONS). Avoid the use of mefenamic acid in patients with advanced renal disease unless the benefits are expected to outweigh the risk of worsening renal function. If mefenamic acid is used in patients with advanced renal disease, monitor patients for signs of worsening renal function.

Hyperkalemia

Increases in serum potassium concentration, including hyperkalemia, have been reported with use of NSAIDs, even in some patients without renal impairment. In patients with normal renal function, these effects have been attributed to a hyporeninemic-hypoaldosteronism state.

Anaphylactic Reactions

Mefenamic acid has been associated with anaphylactic reactions in patients with and without known hypersensitivity to mefenamic acid and in patients with aspirin-sensitive asthma (see CONTRAINDICATIONS, WARNINGS; EXACERBATION OF ASTHMA RELATED TO ASPIRIN SENSITIVITY).

Seek emergency help if anaphylactic reaction occurs.

Exacerbation of Asthma Related to Aspirin Sensitivity

A subpopulation of patients with asthma may have aspirin-sensitive asthma which may include chronic rhinosinusitis complicated by nasal polyps; severe, potentially fatal bronchospasm; and/or intolerance to aspirin and other NSAIDs. Because cross-reactivity between aspirin and other NSAIDs has been reported in such aspirin-sensitive patients, mefenamic acid is contraindicated in patients with this form of aspirin sensitivity

(see CONTRAINDICATIONS). When mefenamic acid is used in patients with pre-existing asthma (without known aspirin sensitivity), monitor patients for changes in the signs and symptoms of asthma.

Serious Skin Reactions

NSAIDs, including mefenamic acid, can cause serious skin adverse reactions such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Inform patients about the signs and symptoms of serious skin reactions and to discontinue the use of mefenamic acid at the first appearance of skin rash or any other sign of hypersensitivity. Mefenamic acid is contraindicated in patients with previous serious skin reactions to NSAIDs (see CONTRAINDICATIONS).

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as mefenamic acid. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection.

Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue mefenamic acid and evaluate the patient immediately.

Fetal Toxicity

Premature Closure of Fetal Ductus Arteriosus

Avoid use of NSAIDs, including mefenamic acid, in pregnant women at about 30 weeks gestation and later. NSAIDs including mefenamic acid, increase the risk of premature closure of the fetal ductus arteriosus at approximately this gestational age.

Oligohydramnios/Neonatal Renal Impairment

Use of NSAIDs, including mefenamic acid, at about 20 weeks gestation or later in pregnancy may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation.

Oligohydramnios is often, but not always, reversible with treatment discontinuation. Complications of prolonged oligohydramnios may, for example, include limb contractures and delayed lung maturation. In some postmarketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.

If NSAID treatment is necessary between about 20 weeks and 30 weeks gestation, limit mefenamic acid use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if mefenamic acid treatment extends beyond 48 hours. Discontinue mefenamic acid if oligohydramnios occurs and follow up according to clinical practice [see PRECAUTIONS; PREGNANCY].

Hematological Toxicity

Anemia has occurred in NSAID-treated patients. This may be due to occult or gross blood loss, fluid retention, or an incompletely described effect on erythropoiesis. If a patient treated with mefenamic acid has any signs or symptoms of anemia, monitor hemoglobin or hematocrit.

NSAIDs, including mefenamic acid, may increase the risk of bleeding events. Co-morbid conditions such as coagulation disorders or concomitant use of warfarin, other anticoagulants, antiplatelet agents (e.g., aspirin), serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) may increase this risk. Monitor these patients for signs of bleeding (see PRECAUTIONS; DRUG INTERACTIONS).

PRECUAUTIONS

General

Mefenamic acid cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to disease exacerbation.

Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids.

Information for Patients

Advise the patient to read the FDA-approved patient labeling (Medication Guide) that accompanies each prescription dispensed. Inform patients, families and their caregivers of the following information before initiating therapy with mefenamic acid and periodically during the course of ongoing therapy.

Cardiovascular Thrombotic Events

Advise patients to be alert for the symptoms of cardiovascular thrombotic events, including chest pain, shortness of breath, weakness, or slurring of speech, and to report any of these symptoms to their healthcare provider immediately (see WARNINGS; CARDIOVASCULAR THROMBOTIC EVENTS).

Gastrointestinal Bleeding, Ulceration, and Perforation

Advise patients to report symptoms of ulcerations and bleeding, including epigastric pain, dyspepsia, melena, and hematemesis to their healthcare provider. In the setting of concomitant use of low-dose aspirin for cardiac prophylaxis, inform patients of the increased risk for and the signs and symptoms of GI bleeding (see WARNINGS; GASTROINTESTINAL BLEEDING, ULCERATION, AND PERFORATION).

Hepatotoxicity

Inform patients of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, pruritus, diarrhea, jaundice, right upper quadrant tenderness, and "flu-like" symptoms). If these occur, instruct patients to stop mefenamic acid and seek immediate medical therapy (see WARNINGS; HEPATOTOXICITY).

Heart Failure and Edema

Advise patients to be alert for the symptoms of congestive heart failure including shortness of breath, unexplained weight gain, or edema and to contact their healthcare

provider if such symptoms occur (see WARNINGS; HEART FAILURE AND EDEMA).

Anaphylactic Reactions

Inform patients of the signs of an anaphylactic reaction (e.g., difficulty breathing, swelling of the face or throat). Instruct patients to seek immediate emergency help if these occur (see CONTRAINDICATIONS, WARNINGS; ANAPHYLACTIC REACTIONS).

Serious Skin Reactions, including DRESS

Advise patients to stop mefenamic acid immediately if they develop any type of rash or fever and to contact their healthcare provider as soon as possible (see WARNINGS).

Female Fertility

Advise females of reproductive potential who desire pregnancy that NSAIDs, including mefenamic acid, may be associated with a reversible delay in ovulation. (see PRECAUTIONS; CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY).

Fetal Toxicity

Inform pregnant women to avoid use of mefenamic acid and other NSAIDs starting at 30 weeks gestation because of the risk of the premature closing of the fetal ductus arteriosus. If treatment with mefenamic acid is needed for a pregnant woman between about 20 to 30 weeks gestation, advise her that she may need to be monitored for oligohydramnios, if treatment continues for longer than 48 hours [see WARNINGS; FETAL TOXICITY, PRECAUTIONS; PREGNANCY].

Avoid Concomitant Use of NSAIDs

Inform patients that the concomitant use of mefenamic acid with other NSAIDs or salicylates (e.g., diflunisal, salsalate) is not recommended due to the increased risk of gastrointestinal toxicity, and little or no increase in efficacy (see WARNINGS; GASTROINTESTINAL BLEEDING, ULCERATION AND PERFORATION, PRECAUTIONS; DRUG INTERACTIONS). Alert patients that NSAIDs may be present in “over the counter” medications for treatment of colds, fever, or insomnia.

Use of NSAIDS and Low-Dose Aspirin

Inform patients not to use low-dose aspirin concomitantly with mefenamic acid until they talk to their healthcare provider (see PRECAUTIONS; DRUG INTERACTIONS).

Masking of Inflammation and Fever

The pharmacological activity of mefenamic acid in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infections.

Laboratory Monitoring

Because serious GI bleeding, hepatotoxicity, and renal injury can occur without warning symptoms or signs, consider monitoring patients on long-term NSAID treatment with a CBC and a chemistry profile checked periodically (see WARNINGS; GASTROINTESTINAL BLEEDING, ULCERATION AND PERFORATION, AND HEPATOTOXICITY).

Drug Interactions

See Table 2 for clinically significant drug interactions with mefenamic acid.

Table 2: Clinically Significant Drug Interactions with Mefenamic Acid

Drugs That Interfere with Hemostasis	
Clinical Impact:	• Mefenamic acid and anticoagulants such as warfarin have a synergistic effect on bleeding. The concomitant use of mefenamic acid and anticoagulants have an increased risk of serious bleeding compared to the use of either drug alone. • Serotonin release by platelets plays an important role in hemostasis. Case-control and cohort epidemiological studies showed that concomitant use of drugs that interfere with serotonin reuptake and an NSAID may potentiate the risk of bleeding more than an NSAID alone.
Intervention:	Monitor patients with concomitant use of mefenamic acid with anticoagulants (e.g., warfarin), antiplatelet agents (e.g., aspirin), selective serotonin reuptake inhibitors (SSRIs), and serotonin norepinephrine reuptake inhibitors (SNRIs) for signs of bleeding (see WARNINGS; HEMATOLOGIC TOXICITY) .
Aspirin	
Clinical Impact:	Controlled clinical studies showed that the concomitant use of NSAIDs and analgesic doses of aspirin does not produce any greater therapeutic effect than the use of NSAIDs alone. In a clinical study, the concomitant use of an NSAID and aspirin was associated with a significantly increased incidence of GI adverse reactions as compared to use of the NSAID alone (see WARNINGS; GASTROINTESTINAL BLEEDING, ULCERATION AND PERFORATION) .
Intervention:	Concomitant use of mefenamic acid and analgesic doses of aspirin is not generally recommended because of the increased risk of bleeding (see WARNINGS; HEMATOLOGIC TOXICITY). Mefenamic acid is not a substitute for low dose aspirin for cardiovascular protection.
ACE Inhibitors, Angiotensin Receptor Blockers, and Beta-Blockers	
Clinical Impact:	• NSAIDs may diminish the antihypertensive effect of angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), or beta-blockers (including propranolol).
	• In patients who are elderly, volume-depleted (including those on diuretic therapy), or have renal impairment, co-administration of an NSAID with ACE inhibitors or ARBs may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible.
Intervention:	• During concomitant use of mefenamic acid and ACE-inhibitors, ARBs, or beta-blockers, monitor blood pressure to ensure that the desired blood pressure is obtained.
	• During concomitant use of mefenamic acid and ACE-inhibitors or ARBs in patients who are elderly, volume-depleted, or have impaired renal function, monitor for signs of worsening renal function (see WARNINGS; RENAL TOXICITY AND HYPERKALEMIA).

	• When these drugs are administered concomitantly, patients should be adequately hydrated. Assess renal function at the beginning of the concomitant treatment and periodically thereafter.
Diuretics	
Clinical Impact:	Clinical studies, as well as post-marketing observations, showed that NSAIDs reduced the natriuretic effect of loop diuretics (e.g., furosemide) and thiazide diuretics in some patients. This effect has been attributed to the NSAID inhibition of renal prostaglandin synthesis.
Intervention	During concomitant use of mefenamic acid with diuretics, observe patients for signs of worsening renal function, in addition to assuring diuretic efficacy including antihypertensive effects (see WARNINGS; RENAL TOXICITY AND HYPERKALEMIA).
Digoxin	
Clinical Impact:	The concomitant use of mefenamic acid with digoxin has been reported to increase the serum concentration and prolong the half-life of digoxin.
Intervention:	During concomitant use of mefenamic acid and digoxin, monitor serum digoxin levels.
Lithium	
Clinical Impact:	NSAIDs have produced elevations in plasma lithium levels and reductions in renal lithium clearance. The mean minimum lithium concentration increased 15%, and the renal clearance decreased by approximately 20%. This effect has been attributed to NSAID inhibition of renal prostaglandin synthesis.
Intervention:	During concomitant use of mefenamic acid and lithium, monitor patients for signs of lithium toxicity.
Methotrexate	
Clinical Impact:	Concomitant use of NSAIDs and methotrexate may increase the risk for methotrexate toxicity (e.g., neutropenia, thrombocytopenia, renal dysfunction).
Intervention:	During concomitant use of mefenamic acid and methotrexate, monitor patients for methotrexate toxicity.
Cyclosporine	
Clinical Impact:	Concomitant use of mefenamic acid and cyclosporine may increase cyclosporine’s nephrotoxicity.
Intervention:	During concomitant use of mefenamic acid and cyclosporine, monitor patients for signs of worsening renal function.
NSAIDs and Salicylates	
Clinical Impact:	Concomitant use of mefenamic acid with other NSAIDs or salicylates (e.g., diflunisal, salsalate) increases the risk of GI toxicity, with little or no increase in efficacy (see WARNINGS; Gastrointestinal Bleeding, Ulceration and Perforation).
Intervention:	The concomitant use of mefenamic acid with other NSAIDs or salicylates is not recommended.
Pemetrexed	
Clinical Impact:	Concomitant use of mefenamic acid and pemetrexed may increase the risk of pemetrexedassociated myelosuppression, renal, and GI toxicity (see the pemetrexed prescribing information).

Intervention:	During concomitant use of mefenamic acid and pemetrexed, in patients with renal impairment whose creatinine clearance ranges from 45 to 79 mL/min, monitor for myelosuppression, renal and GI toxicity.
	NSAIDs with short elimination half-lives (e.g., diclofenac, indomethacin) should be avoided for a period of two days before, the day of, and two days following administration of pemetrexed.
	In the absence of data regarding potential interaction between pemetrexed and NSAIDs with longer half-lives (e.g., meloxicam, nabumetone), patients taking these NSAIDs should interrupt dosing for at least five days before, the day of, and two days following pemetrexed administration.
Antacid	
Clinical Impact:	In a single dose study (n= 6), ingestion of an antacid containing 1.7-gram of magnesium hydroxide with 500-mg of mefenamic acid increased the C max and AUC of mefenamic acid by 125% and 36%, respectively.
Intervention:	Concomitant use of mefenamic acid and antacids is not generally recommended because of possible increased adverse events.

Drug/Laboratory Test Interactions

Mefenamic acid may prolong prothrombin time. Therefore, when the drug is administered to patients receiving oral anticoagulant drugs, frequent monitoring of prothrombin time is necessary.

A false-positive reaction for urinary bile, using the diazo tablet test, may result after mefenamic acid administration. If biliuria is suspected, other diagnostic procedures, such as the Harrison spot test, should be performed.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Long-term studies in animals to evaluate the carcinogenic potential of mefenamic acid have not been conducted.

Mutagenesis

Studies to evaluate the mutagenic potential of mefenamic acid have not been completed.

Impairment of Fertility

Dietary administration of mefenamic acid to male rats 61 days- and to female rats 15 days- prior to mating through to Gestation Day (GD) 21 at a dose of 155 mg/kg/day (equivalent to the Maximum Recommended Human Dose [MRHD] of 1500 mg/day on a mg/m 2 basis) resulted in decreased corpora lutea.

In another study, rats administered up to 10-times a human dose of 250 mg showed decreased fertility.

Pregnancy

Risk Summary

Use of NSAIDs, including mefenamic acid, can cause premature closure of the fetal ductus arteriosus and fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, limit dose and duration of

mefenamic acid use between about 20 and 30 weeks of gestation, and avoid mefenamic acid use at about 30 weeks of gestation and later in pregnancy [see WARNINGS; FETAL TOXICITY].

Premature Closure of Fetal Ductus Arteriosus

Use of NSAIDs, including mefenamic acid, at about 30 weeks gestation or later in pregnancy increases the risk of premature closure of the fetal ductus arteriosus.

Oligohydramnios/Neonatal Renal Impairment

Use of NSAIDs at about 20 weeks gestation or later in pregnancy has been associated with cases of fetal renal dysfunction leading to oligohydramnios, and in some cases, neonatal renal impairment.

Data from observational studies regarding other potential embryofetal risks of NSAID use in women in the first or second trimesters of pregnancy are inconclusive. Based on animal data, prostaglandins have been shown to have an important role in endometrial vascular permeability, blastocyst implantation, and decidualization. In animal studies, administration of prostaglandin synthesis inhibitors such as mefenamic acid, resulted in increased pre- and post-implantation loss.

Prostaglandins also have been shown to have an important role in fetal kidney development. In published animal studies, prostaglandin synthesis inhibitors have been reported to impair kidney development when administered at clinically relevant doses.

The estimated background risk of major birth defects and miscarriage for the indicated population(s) is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Premature Closure of Fetal Ductus Arteriosus:

Avoid use of NSAIDs in women at about 30 weeks gestation and later in pregnancy, because NSAIDs, including mefenamic acid, can cause premature closure of the fetal ductus arteriosus (see WARNINGS; FETAL TOXICITY) .

Oligohydramnios/Neonatal Renal Impairment:

If an NSAID is necessary at about 20 weeks gestation or later in pregnancy, limit the use to the lowest effective dose and shortest duration possible. If mefenamic acid treatment extends beyond 48 hours, consider monitoring with ultrasound for oligohydramnios. If oligohydramnios occurs, discontinue mefenamic acid and follow up according to clinical practice (see WARNINGS; FETAL TOXICITY) .

Data

Human Data

Premature Closure of Fetal Ductus Arteriosus:

Published literature reports that the use of NSAIDs at about 30 weeks of gestation and later in pregnancy may cause premature closure of the fetal ductus arteriosus.

Oligohydramnios/Neonatal Renal Impairment:

Published studies and postmarketing reports describe maternal NSAID use at about 20 weeks gestation or later in pregnancy associated with fetal renal dysfunction leading to oligohydramnios, and in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. In many cases, but not all, the decrease in amniotic fluid was transient and reversible with cessation of the drug. There have been a limited number of case reports of maternal NSAID use and neonatal renal dysfunction without oligohydramnios, some of which were irreversible. Some cases of such as exchange transfusion or dialysis.

Methodological limitations of these postmarketing studies and reports include lack of a control group; limited information regarding dose, duration, and timing of drug exposure; and concomitant use of other medications. These limitations preclude establishing a reliable estimate of the risk of adverse fetal and neonatal outcomes with maternal NSAID use. Because the published safety data on neonatal outcomes involved mostly preterm infants, the generalizability of certain reported risks to the full-term infant exposed to NSAIDs through maternal use is uncertain.

Animal data

Pregnant rats administered 249 mg/kg of mefenamic acid (1.6-times the MRHD of 1500 mg/day on a mg/m 2 basis) from GD 6 to GD 15 did not result in any clear adverse developmental effects.

Pregnant rabbits given 50 mg/kg of mefenamic acid (0.6-times the MRHD on a mg/m 2 basis) from GD 6 to GD 18 did not result in any clear treatment-related adverse developmental effects. However, incidences of resorption were greater in treated compared to control animals. This dose was associated with some evidence of maternal toxicity with 4 of 18 rabbits exhibiting diarrhea and weight loss.

Dietary administration of mefenamic acid at a dose of 181 mg/kg (1.2-times the MRHD on a mg/m 2 basis) to pregnant rats from GD 15 to weaning resulted in an increased incidence of perinatal death. Treated dams were associated with decreased weight gain and delayed parturition. In another study, dietary administration of mefenamic acid at a dose of 155 mg/kg (equivalent to the MRHD of 1500 mg/day on a mg/m 2 basis) to females 15 days prior to mating through to weaning resulted in smaller average litter sizes and higher incidence of perinatal death.

Labor and Delivery

In rat studies with NSAIDs, as with other drugs known to inhibit prostaglandin synthesis, an increased incidence of dystocia, delayed parturition, decreased pup survival occurred and increased the incidence of stillbirth. The effects of mefenamic acid on labor and delivery in pregnant women are unknown.

Nursing Mothers

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

Infertility

Females

Based on the mechanism of action, the use of prostaglandin-mediated NSAIDs, including mefenamic acid may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in some women. Published animal studies have shown that administration of prostaglandin synthesis inhibitors has the potential to disrupt prostaglandin in mediated follicular rupture required for ovulation. Small studies in women treated with NSAIDs have also shown a reversible delay in ovulation. Consider withdrawal of NSAIDs, including mefenamic acid, in women who have difficulties conceiving or who are undergoing investigation of infertility.

Pediatric Use

Safety and effectiveness in pediatric patients below the age of 14 have not been established.

Geriatric Use

Elderly patients, compared to younger patients, are at greater risk for NSAID-associated serious cardiovascular, gastrointestinal, and/or renal adverse reactions. If the anticipated benefit for the elderly patient outweighs these potential risks, start dosing at the low end of the dosing range, and monitor patients for adverse effects (see WARNINGS; CARDIOVASCULAR THROMBOTIC EVENTS, GASTROINTESTINAL BLEEDING, ULCERATION, AND PERFORATION, HEPATOTOXICITY, RENAL TOXICITY AND HYPERKALEMIA, PRECAUTIONS; LABORATORY MONITORING).

Clinical studies of mefenamic acid did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. As with any NSAID, caution should be exercised in treating the elderly (65 years and older).

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (See CLINICAL PHARMACOLOGY, ADVERSE REACTIONS)

The following adverse reactions are discussed in greater detail in other sections of the labeling:

- Cardiovascular Thrombotic Events (see WARNINGS)
- GI Bleeding, Ulceration and Perforation (see WARNINGS)
- Hepatotoxicity (see WARNINGS)
- Hypertension (see WARNINGS)
- Heart Failure and Edema (see WARNINGS)
- Renal Toxicity and Hyperkalemia (see WARNINGS)
- Anaphylactic Reactions (see WARNINGS)
- Serious Skin Reactions (see WARNINGS)
- Hematologic Toxicity (see WARNINGS)

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In patients taking mefenamic acid or other NSAIDs, the most frequently reported adverse experiences occurring in approximately 1 to 10% of patients are:

Gastrointestinal experiences including - abdominal pain, constipation, diarrhea, dyspepsia, flatulence, gross bleeding/perforation, heartburn, nausea, GI ulcers (gastric/duodenal), vomiting, abnormal renal function, anemia, dizziness, edema, elevated liver enzymes, headaches, increased bleeding time, pruritus, rashes, tinnitus

Additional adverse experiences reported occasionally and listed here by body system include:

Body as a whole - fever, infection, sepsis

Cardiovascular system - congestive heart failure, hypertension, tachycardia, syncope

Digestive system - dry mouth, esophagitis, gastric/peptic ulcers, gastritis, gastrointestinal bleeding, glossitis, hematemesis, hepatitis, jaundice

Hemic and lymphatic system - ecchymosis, eosinophilia, leukopenia, melena, purpura, rectal bleeding, stomatitis, thrombocytopenia

Metabolic and nutritional - weight changes

Nervous system - anxiety, asthenia, confusion, depression, dream abnormalities, drowsiness; insomnia, malaise, nervousness, paresthesia, somnolence, tremors, vertigo

Respiratory system - asthma, dyspnea

Skin and appendages - alopecia, photosensitivity, pruritus, sweat

Special senses - blurred vision

Urogenital system - cystitis, dysuria, hematuria, interstitial nephritis, oliguria/polyuria, proteinuria, renal failure

Other adverse reactions, which occur rarely are:

Body as a whole - anaphylactoid reactions, appetite changes, death

Cardiovascular system - arrhythmia, hypotension, myocardial infarction, palpitations, vasculitis Digestive system - eructation, liver failure, pancreatitis

Hemic and lymphatic system - agranulocytosis, hemolytic anemia, aplastic anemia, lymph adenopathy, pancytopenia

Metabolic and nutritional - hyperglycemia

Nervous system - convulsions, coma, hallucinations, meningitis

Respiratory - respiratory depression, pneumonia

Skin and appendages - angioedema, toxic epidermal necrosis, erythema multiforme, exfoliative dermatitis, Stevens - Johnson syndrome, urticaria

Special senses - conjunctivitis, hearing impairment

To report SUSPECTED ADVERSE REACTIONS, contact Micro Labs USA, Inc. at 1-855-839-8195 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Symptoms following acute NSAID overdosages have been typically limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which have been generally reversible

with supportive care. Gastrointestinal bleeding has occurred. Hypertension, acute renal failure, respiratory depression and coma have occurred, but were rare (see WARNINGS; CARDIOVASCULAR THROMBOTIC EVENTS, GASTROINTESTINAL BLEEDING, ULCERATION, AND PERFORATION, HYPERTENSION, RENAL TOXICITY AND HYPERKALEMIA).

Manage patients with symptomatic and supportive care following an NSAID overdosage. There are no specific antidotes. Consider emesis and/or activated charcoal (60 to 100 grams in adults, 1 to 2 grams per kg of body weight in pediatric patients) and/or osmotic cathartic in symptomatic patients seen within four hours of ingestion or in patients with a large overdose (5 to 10 times the recommended dosage). Forced diuresis, alkalinization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

For additional information about overdosage treatment, contact a poison control center (1-800-222-1222).

Carefully consider the potential benefits and risks of mefenamic acid and other treatment options before deciding to use mefenamic acid. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see WARNINGS; GASTROINTESTINAL BLEEDING, ULCERATION, AND PERFORATION).

After observing the response to initial therapy with mefenamic acid, the dose and frequency should be adjusted to suit an individual patient's needs.

For the relief of acute pain in adults and adolescents ≥14 years of age, the recommended dose is 500 mg as an initial dose followed by 250 mg every 6 hours as needed, usually not to exceed one week.

For the treatment of primary dysmenorrhea, the recommended dose is 500 mg as an initial dose followed by 250 mg every 6 hours, given orally, starting with the onset of bleeding and associated symptoms. Clinical studies indicate that effective treatment can be initiated with the start of menses and should not be necessary for more than 2 to 3 days.

Mefenamic Acid Capsules USP 250 mg are Size ‘1’ yellow-yellow capsules with ‘ML’ imprinted on the cap & ‘250’ imprinted on the body. They are supplied as follows:

Bottles of 30 Capsules NDC: 80425-0306-01

Bottles of 60 Capsules NDC: 80425-0306-02

Bottles of 90 Capsules NDC: 80425-0306-03

Dispense in a tight container as defined in the USP.

Storage

Store at room temperature 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

For inquiries call 1-855-839-8195

Manufactured by:
Micro Labs Limited
Goa- 403 722, INDIA.

Manufactured for:

Micro Labs USA, Inc.
Somerset, NJ 08873

Medication Guide for Nonsteroidal Anti-inflammatory Drugs (NSAIDS)

Mefenamic Acid (mef-e-NAM-ik AS-id) Capsules, USP 250 mg

What is the most important information I should know about medicines called Nonsteroidal Anti-inflammatory Drugs (NSAIDs)?

NSAID can cause serious side effects, including:

- Increase risk of a heart attack or stroke that can lead to death. This risk may happen early in treatment and may increase:
- with increasing doses of NSAIDs
- with longer use of NSAIDs

Do not take NSAIDs right before or after a heart surgery called a “coronary artery bypass graft (CABG)". Avoid taking NSAIDs after a recent heart attack, unless your healthcare provider tells you to. You may have an increased risk of another heart attack if you take NSAIDs after a recent heart attack.

- Increase risk of bleeding, ulcers and tears (perforation) of the esophagus (tube leading from the mouth to the stomach), stomach and intestines:

- anytime during use
- without warning symptoms
- that may cause death

The risk of getting an ulcer or bleeding increases with:

- past history of stomach ulcers, or stomach or intestinal bleeding with use of NSAIDs
- taking medicines called “corticosteroids”, “anticoagulants”, “SSRIs”, or “SNRIs”
- increasing doses of NSAIDs
- older age
- longer use of NSAIDs
- poor health
- smoking
- advanced liver disease
- drinking alcohol
- bleeding problems

NSAID should only be used:

- exactly as prescribed
- at the lowest dose possible for your treatment
- or the shortest time needed

What are NSAIDs?

NSAIDs are used to treat pain and redness, swelling, and heat (inflammation) from medical conditions such as different types of arthritis, menstrual cramps, and other types of short-term pain.

Who should not take NSAIDs? Do not take NSAIDs:

- if you have had an asthma attack, hives, or other allergic reaction with aspirin or any other NSAIDs.
- right before or after heart bypass surgery.

Before taking NSAIDs, tell our healthcare provider about all of your medical conditions, including if you:

- have liver or kidney problems
- have high blood pressure
- have asthma
- are pregnant or plan to become pregnant. Taking NSAIDs at about 20 weeks of pregnancy or later may harm your unborn baby. If you need to take NSAIDs for more than 2 days when you are between 20 and 30 weeks of pregnancy, your healthcare provider may need to monitor the amount of fluid in your womb around your baby. You should not take NSAIDs after about 30 weeks of pregnancy
- are breastfeeding or plan to breastfeed

Tell your healthcare provider about all of the medicines you take, including prescription or over-the-counter medicines, vitamins, or herbal supplements. NSAIDs and some other medicines can interact with each other and cause serious side effects. Do not start taking any new medicine without talking to your healthcare provider first.

What are the possible side effects of NSAIDs?

NSAIDs can cause serious side effects, including:

See “What is the most important information I should know about medicines called Nonsteroidal Anti-inflammatory Drugs (NSAIDs)?”

- new or worse high blood pressure
- heart failure
- liver problems including liver failure
- kidney problem including kidney failure
- low red blood cells (anemia)
- life-threatening skin reactions
- life-threatening allergic reactions

- Other side effects if NSAIDs include: stomach pain, constipation, diarrhea, gas, heartburn, nausea, vomiting, and dizziness.

Get emergency help right away if you get any of the following symptoms:

shortness of breath or trouble breathing

slurred speech

chest pain
swelling of the face or throat

weakness in one part or side of your body

Stop taking your NSAID and call your healthcare provider right away if you get any of the following symptoms:

- nausea
- vomit blood
- more tired or weaker than usual

- there is blood in the bowel movement or it is black and sticky like tar
- diarrhea
- unusual weight gain
- itching
- skin rash or blisters with fever
- your skin or eyes look yellow
- swelling of the arms, legs, hands, and feet
- indigestion or stomach pain
- flu-like symptoms

If you take too much of your NSAID, call your healthcare provider or get medical help right away.

These are not all of the possible side effects of NSAIDs. For more information, ask your healthcare provider or pharmacist about NSAIDs. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Other information about NSAIDs

Aspirin is an NSAID medicine but it does not increase the chance of a heart attack. Aspirin can cause bleeding in the brain, stomach, and intestines. Aspirin can also cause ulcers in the stomach and intestines.
Some NSAIDs are sold in lower doses without a prescription (over-the-counter). Talk to your healthcare provider before using over-the-counter NSAID for more than 10 days.

General information about the safe and effective use of NSAIDs

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use NSAIDs for a condition for which it was not prescribed. Do not give NSAIDs to other people, even if they have the same symptoms that you have. It may harm them.

If you would like more information about NSAIDs, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about NSAIDs that is written for health professionals.

For more information, call 1-855-839-8195

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by:
Micro Labs Limited
Goa- 403 722, INDIA.

Manufactured for:
Micro Labs USA, Inc.
Somerset, NJ 08873

Rev.11/2021

MEFENAMIC ACID

mefenamic acid capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:80425-0306(NDC:42571-258)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
MEFENAMIC ACID (UNII: 367589PJ2C) (MEFENAMIC ACID - UNII:367589PJ2C)	MEFENAMIC ACID	250 mg

Product Characteristics

Color	yellow	**Score**	no score
Shape	CAPSULE	**Size**	19mm
Flavor		**Imprint Code**	ML;250
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:80425-	30 in 1 BOTTLE; Type 0: Not a Combination	04/06/2023	

1	0306-1	Product	04/06/2023	
2	NDC:80425-0306-2	60 in 1 BOTTLE; Type 0: Not a Combination Product	04/06/2023	
3	NDC:80425-0306-3	90 in 1 BOTTLE; Type 0: Not a Combination Product	04/06/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA090562	04/06/2023	

Labeler - Advanced Rx Pharmacy of Tennessee, LLC (117023142)

Establishment

Name	Address	ID/FEI	Business Operations
Advanced Rx Pharmacy of Tennessee, LLC		117023142	repack(80425-0306)

Revised: 4/2023 Advanced Rx Pharmacy of Tennessee, LLC