HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use MEFENAMIC ACID CAPSULES safely and effectively. See full prescribing information for MEFENAMIC ACID CAPSULES.

MEFENAMIC acid capsules, for oral use. Initial U.S. Approval: 1967

WARNING: RISK OF SERIOUS CARDIOVASCULAR and GASTROINTESTINAL EVENTS
See full prescribing information for complete boxed warning.

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 and Precautions (5.1)].**
- **Mefenamic acid is contraindicated in the setting of coronary artery bypass graft (CABG) surgery [see Warnings and Precautions (5.1)].**

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 and Precautions (5.2)].**

----------INDICATIONS AND USAGE----------
Mefenamic acid capsules are nonsteroidal anti-inflammatory drug indicated for:
- For management of mild to moderate pain in patient 14 years of age and older, when therapy will not exceed one week (7 days). (1.1)
- For treatment of primary dysmenorrhea. (1.2)

----------DOSAGE AND ADMINISTRATION----------
- Adults and adolescents 14 years of age and older: 500 mg given orally as an initial dose followed by 250 mg every 6 hours as needed (2.2)
- For the treatment of primary dysmenorrhea: 500 mg given orally as an initial dose followed by 250 mg every 6 hours (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
- Capsule: 250 mg of mefenamic acid (3)

----------CONTRAINDICATIONS----------
- Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to mefenamic acid or any components of the drug product (4)
- 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 (4)
- In the setting of coronary artery bypass graft (CABG) surgery (4)

----------WARNINGS AND PRECAUTIONS----------
Hepatotoxicity: Inform patients of warning signs and symptoms of hepatotoxicity. Discontinue if abnormal liver tests persist or worsen or if clinical signs and symptoms of liver disease develop. (5.3)
Hypertension: Patients taking some antihypertensive medications may have impaired response to these therapies when taking NSAIDs. Monitor blood pressure. (5.4, 7)
Heart Failure and Edema: Avoid use of mefenamic acid in patients with severe heart failure unless benefits are expected to outweigh risk of worsening heart failure. (5.5)
Renal Toxicity: Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia. Avoid use of mefenamic acid in patients with advanced renal disease unless benefits are expected to outweigh risk of worsening renal function. (5.6)
Anaphylactic Reactions: Seek emergency help if an anaphylactic reaction occurs. (5.7)
Exacerbation of Asthma Related to Aspirin Sensitivity: Mefenamic acid iscontraindicated in patients with aspirin-sensitive asthma. Monitor patients with preexisting asthma (without aspirin sensitivity). (5.8)
Serious Skin Reactions: Discontinue mefenamic acid at first appearance of skin rash or other signs of hypersensitivity. (5.9)
Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS): Discontinue and evaluate clinically. (5.10)
Fetal Toxicity: Limit use of NSAIDs, including mefenamic acid, between about 20 to 30 weeks in pregnancy due to the risk of oligohydramnios/fetal renal dysfunction. Avoid use of NSAIDs in women at about 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/fetal renal dysfunction and premature closure of the fetal ductus arteriosus. (5.11, 8.1)
Hematologic Toxicity: Monitor hemoglobin or hematocrit in patients with any signs or symptoms of anemia. (5.12, 7)

----------ADVERSE REACTIONS----------
In patients taking mefenamic acid or other NSAIDs, the most frequently reported adverse reactions occurring in approximately 1 to 10 % of patients are: 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 (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Lupin Pharmaceuticals, Inc. at 1-800-399-2561 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------USE IN SPECIFIC POPULATIONS----------
Infertility: NSAIDs are associated with reversible infertility. Consider withdrawal of mefenamic acid in women who have difficulty conceiving. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 02/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

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 and Precautions (5.1)]*.**
- **Mefenamic acid is contraindicated in the setting of coronary artery bypass graft (CABG) surgery *[see Contraindications (4), see Warnings and Precautions (5.1)]*.**

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 and Precautions (5.2)]*.**

1 INDICATIONS AND USAGE

1.1 Mild to Moderate Pain

Mefenamic acid capsules are indicated for management of mild to moderate pain in adults and pediatric patients 14 years of age and older, when therapy will not exceed one week (7 days).

1.2 Dysmenorrhea

Mefenamic acid capsules are indicated for treatment of primary dysmenorrhea.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Information

Carefully consider the potential benefits and risks of mefenamic acid capsules and other treatment options before deciding to use mefenamic acid capsules. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals *[see Warnings and Precautions (5.2)]*.

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

2.2 For the Management of Mild to Moderate Pain

The recommended dosage in adults and pediatric patients 14 years of age and older is 500 mg given orally as an initial dose followed by 250 mg every 6 hours as needed.

2.3 Dysmenorrhea

The recommended dose is 500 mg given orally as an initial dose followed by 250 mg every 6 hours starting with the onset of bleeding and associated symptoms.

3 DOSAGE FORMS AND STRENGTHS

250 mg size '1' capsules having ivory cap and ivory body imprinted with "LU" on cap and "R31" on body in black ink.

4 CONTRAINDICATIONS

Mefenamic acid capsules are 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 and Precautions (5.7)]*.
- 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 and Precautions (5.7, 5.8, 5.9)]*.
- In the setting of coronary artery bypass graft (CABG) surgery *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 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 and Precautions (5.2)]*.

<u>Status Post Coronary Artery Bypass Graft (CABG) Surgery</u>

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 (4)]*.

<u>Post-MI Patients</u>

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 capsules 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.

5.2 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, anti-platelet drugs (such as 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 Drug Interactions (7.1)]*.

5.3 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 capsules immediately, and perform a clinical evaluation of the patient.

5.4 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 Drug Interactions (7.1)]*.

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

5.5 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 non-selective 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 Drug Interactions (7.1)]*.

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 capsules are used in patients with severe heart failure, monitor patients for signs of worsening heart failure.

5.6 Renal Toxicity and Hyperkalemia

Renal Toxicity

Long-term administration of NSAIDs, including mefenamic acid, 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 Drug Interactions (7.1)]*.

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.

5.7 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 (4); Warnings and Precautions (5.7)]*.

Advise patients to seek emergency help if anaphylactic reaction occurs.

5.8 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 (4)]*. 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.

5.9 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**.** NSAIDs can also cause fixed drug eruption (FDE). FDE may present as a more severe variant known as generalized bullous fixed drug eruption (GBFDE), which can be life-threatening. 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 capsules 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 (4)]*.

5.10 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.

5.11 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 Use in Specific Populations (8.1)]*.

5.12 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 capsules 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 Drug Interactions (7.1)]*.

5.13 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.

5.14 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 and Precautions (5.2, 5.3, 5.6)]*.

6 ADVERSE REACTIONS

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

- Cardiovascular Thrombotic Events *[see Warnings and Precautions (5.1)]*
- GI Bleeding, Ulceration and Perforation *[see Warnings and Precautions (5.2)]*
- Hepatotoxicity *[see Warnings and Precautions (5.3)]*
- Hypertension *[see Warnings and Precautions (5.4)]*
- Heart Failure and Edema *[see Warnings and Precautions (5.5)]*

- Renal Toxicity and Hyperkalemia *[see Warnings and Precautions (5.6)]*
- Anaphylactic Reactions *[see Warnings and Precautions (5.7)]*
- Serious Skin Reactions *[see Warnings and Precautions (5.9, 5.10)]*
- Hematologic Toxicity *[see Warnings and Precautions (5.12)]*

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.

The following adverse reactions associated with the use of mefenamic acid were identified in clinical studies or post- marketing reports. Because some of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure

In patients taking mefenamic acid or other NSAIDs, the most frequently reported adverse reactions occurring in approximately 1 to10 % of patients are:
Gastrointestinal - Abdominal pain, constipation, diarrhea, dyspepsia, flatulence, gross bleeding/perforation, heartburn, nausea, GI ulcers (gastric/duodenal), vomiting

Auditory System - Tinnitus

Genitourinary System - Abnormal renal function

Hepatic System - Elevated liver enzymes

Dermatologic - Pruritus, rashes

Cardiovascular - Anemia, edema

Central Nervous System - Dizziness, headache

Hematopoetic and lymphatic system - Increased bleeding time

Additional adverse experiences reported less frequently and listed here by body system include: General - anaphylactoid reactions, appetite changes, death, fever, infection, sepsis

Cardiovascular - congestive heart failure, hypertension, tachycardia, syncope arrhythmia, hypotension, myocardial infarction, palpitations, vasculitis

Gastrointestinal system - dry mouth, esophagitis, gastric/peptic ulcers, gastritis, gastrointestinal bleeding, glossitis, hematemesis, hepatitis, jaundice, eructation, liver failure, pancreatitis

Hematopoetic and lymphatic system - ecchymosis, eosinophilia, leukopenia, melena, purpura, rectal bleeding, stomatitis, thrombocytopenia, agranulocytosis, hemolytic anemia, aplastic anemia, lymph-adenopathy, pancytopenia

Metabolic - weight changes, hyperglycemia

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

convulsions, coma, hallucinations, meningitis
Respiratory system - asthma, dyspnea, respiratory depression, pneumonia

Dermatologic - alopecia, photosensitivity, pruritus, sweat, angioedema, toxic epidermal necrosis, erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, fixed drug eruption (FDE), urticaria

Special senses - blurred vision, conjunctivitis, hearing impairment

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

7 DRUG INTERACTIONS

7.1 Drug Interactions

See Table 1 for clinically significant drug interactions with mefenamic acid.

Table 1: 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 and Precautions (5.12)]*.
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 and Precautions (5.2)]*.
Intervention:	Concomitant use of mefenamic acid and analgesic doses of aspirin is not generally recommended because of the increased risk of bleeding *[see Warnings and Precautions (5.12)]*. 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 and Precautions (5.6)]*. 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 and Precautions (5.6)]*.
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. This effect has been attributed to NSAID inhibition of renal prostaglandin synthesis *[See Clinical Pharmacology (12.3)]*.
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 and Precautions (5.2)]*.
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 pemetrexed- associated 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:	Concomitant ingestion of antacids containing magnesium hydroxide has been shown to significantly increase the rate and extent of mefenamic acid absorption *[See Clinical Pharmacology (12.3)]*
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.

8 USE IN SPECIFIC POPULATIONS

8.1 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 Clinical Considerations, Data)*.

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. In animal reproduction studies, administration of mefenamic acid to pregnant rats during organogenesis through lactation resulted in perinatal death and smaller litter sizes at exposures comparable to the Maximum Recommended Human Dose (MRHD) *(see Data)*. 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 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 capsules, can cause premature closure of the fetal ductus arteriosus *(see Data)*.

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 capsules and follow up according to clinical practice *(see Data)*.

Labor or Delivery
There are no studies on the effects of mefenamic acid during labor or delivery. In animal studies, NSAIDs, including mefenamic acid, inhibit prostaglandin synthesis, cause delayed parturition, and increase the incidence of stillbirth.

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 Gestation Day (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.

8.2 Lactation

Risk Summary

Mefenamic acid is present in human milk in low amounts and may be transferred to breastfed infants. There are no available data on the effects of mefenamic acid on the breastfed infant or on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for mefenamic acid and any potential adverse effects on the breastfed infant from the mefenamic acid or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

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.

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. Published animal studies have shown that administration of prostaglandin synthesis inhibitors has the potential to disrupt prostaglandin in mediated follicular rupture required for ovulation. Rats administered mefenamic acid resulted in decreased fertility *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and effectiveness of mefenamic acid have been established for management of mild to moderate pain in pediatric patients 14 years of age and older.

The safety and effectiveness of mefenamic acid have been established for treatment of primary dysmenorrhea in pediatric patients.

The safety and effectiveness of mefenamic acid have not been established for management of mild to moderate pain in pediatric patients less than 14 years of age.

8.5 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 and Precautions (5.1, 5.2, 5.3, 5.6, 5.14)]*.

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).

Mefenamic acid 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 Warnings and Precautions (5.1, 5.2, 5.3, 5.6, 5.14), Clinical Pharmacology (12.2), Adverse Reactions (7.1)]*.

8.6 Renal Impairment

The renal effects of mefenamic acid capsules may hasten the progression of renal dysfunction in patients with pre-existing renal disease.

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 capsule should not be administered to patients with pre-existing renal disease or in patients with significantly impaired renal function *[see Warnings and Precautions (5.6)]*.

8.7 Hepatic Impairment

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 and Precautions (5.3)]*.

10 OVERDOSAGE

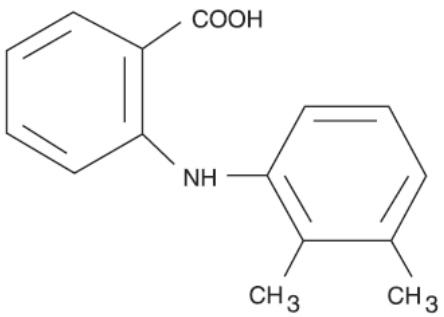
Symptoms following acute NSAID overdosages have been typically limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which have been generally reversible with supportive care. Gastrointestinal bleeding has occurred. Hypertension, acute renal failure, respiratory depression, and coma have occurred but were rare *[see Warnings and Precautions (5.1, 5.2, 5.4, 5.6)].*

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 Help Line (1-800-222-1222).

11 DESCRIPTION

Mefenamic acid capsules USP contains active moiety mefenamic acid, which is a member of the fenamate group of nonsteroidal anti-inflammatory drugs (NSAIDs). The chemical name of mefenamic acid is N-2,3-xylylanthranilic acid. The molecular weight is 241.29 g/mol. Its molecular formula is $C_{15}H_{15}N0_2$ and the structural formula of mefenamic acid is:



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.

Mefenamic acid capsules are for oral administration. Each capsule contains 250 mg of mefenamic acid, lactose monohydrate and magnesium stearate. The capsule shell contains gelatin, sodium lauryl sulfate, titanium dioxide, D&C yellow No. 10, FD&C yellow No. 6 and FD&C red No. 3.

12 CLINICAL PHARMACOLOGY

12.1 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.

12.3 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. 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.

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 (Vz_{ss}/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 Use in Specific Populations (8.2)]*.

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. The mefenamic acid glucuronide may bind irreversibly to plasma proteins. 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.

Table 2. 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)	21.23	38
Apparent volume of distribution; Vz/F (L/kg)	1.06	60
Half-life; $t_{½}$ (hrs)	2 to 4	N/A

Specific Populations

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

*Hepatic Impairment***:** Mefenamic acid pharmacokinetics have not been studied in patients with hepatic dysfunction.

*Renal Impairment***:** Mefenamic acid pharmacokinetics have not been investigated in subjects with renal insufficiency.

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 1 for clinically significant drug interactions of NSAIDs with aspirin *[see Drug Interactions (7.1)]*.

Antacid: 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.

Lithium: The mean minimum lithium concentration increased 15 %, and the renal clearance decreased by approximately 20 %.

13 NONCLINICAL TOXICOLOGY

13.1 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.

14 CLINICAL STUDIES

14.1 Treatment of Primary Spasmodic Dysmenorrhea

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. Patients in the mefenamic acid group had statistically significantly better results compared to placebo on the efficacy parameters (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).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Mefenamic acid capsules USP, 250 mg are available as size ‘1’ capsules having ivory cap and ivory body imprinted with “LU” on cap and “R31” on body in black ink, containing white to off white granular powder.

They are supplied as follows:

NDC 68180-185-06 Bottles of 30’s

Dispense in a tight container as defined in the USP.

16.2 Storage and Handling

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

17 PATIENT COUNSELING INFORMATION

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 capsules 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 and Precautions (5.1)]*.

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 and Precautions (5.2)]*.

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 capsules and seek immediate medical therapy *[see Warnings and Precautions (5.3)]*.

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 and Precautions (5.5)]*.

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 (4), Warnings and Precautions (5.7)]*.

Serious Skin Reactions, including DRESS

Advise patients to stop mefenamic acid capsules immediately if they develop any type of rash or fever and to contact their healthcare provider as soon as possible *[see Warnings and Precautions (5.9)]*.

Female Fertility

Advise females of reproductive potential who desire pregnancy that NSAIDs, including mefenamic acid capsules, may be associated with a reversible delay in ovulation. *[see Use in Specific Populations (8.3)]*.

Fetal Toxicity

Inform pregnant women to avoid use of mefenamic acid capsules 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 capsules 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 and Precautions (5.11), Use in Specific Populations (8.1)]*.

Avoid Concomitant Use of NSAIDs

Inform patients that the concomitant use of mefenamic acid capsules 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 and Precautions (5.2), Drug Interactions (7.1)]*. 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 capsules until they talk to their healthcare provider *[see Drug Interactions (7.1)]*.

Manufactured for:

Lupin Pharmaceuticals, Inc.

Naples, FL 34108

United States

Manufactured by:

Lupin Limited

Goa 403 722

INDIA

Revised: February 2026 ID: 282951

Medication Guide
Mefenamic (me-fe-NAM-ik) Acid Capsules USP

Mefenamic acid capsules are prescription medicine that contains mefenamic acid (a nonsteroidal anti-inflammatory drug [NSAID]).

What is the most important information I should know about mefenamic acid capsules, and medicines called nonsteroidal anti-inflammatory drugs (NSAIDs)?

Mefenamic acid capsules may cause serious side effects, including:

- **Increased 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 mefenamic acid capsules right before or after a heart surgery called a "coronary artery bypass graft (CABG)". Avoid taking mefenamic acid capsules 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 mefenamic acid capsules after a recent heart attack.

- **Increased 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 in the drug classes of corticosteroids, antiplatelets (such as aspirin), anticoagulants, selective serotonin reuptake inhibitors (SSRIs), and serotonin norepinephrine reuptake inhibitors (SNRIs)
- increasing doses of NSAIDs
- longer use of NSAIDs
- smoking
- drinking alcohol
- older age
- poor health
- advanced liver disease
- bleeding problems

Mefenamic acid capsules should only be used:

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

What are mefenamic acid capsules?

Mefenamic acid capsules are prescription medicine used:

- for the management of mild to moderate pain in adults and children 14 years of age and older, when your treatment will not be longer than 1 week (7 days).
- for the treatment of menstrual cramps.

It is not known if mefenamic acid capsules are safe and effective for the management of mild to moderate pain in children less than 14 years of age.

Who should not take mefenamic acid capsules?

Do not take mefenamic acid capsules:

- if you are allergic to mefenamic acid or to any of the ingredients in mefenamic acid capsules. See the end of this Medication Guide for a complete of ingredients in mefenamic acid capsules.
- if you have had an asthma attack, hives, or other allergic reaction after taking aspirin or any other NSAIDs.
- right before or after heart bypass surgery.

Before taking mefenamic acid capsules, tell your healthcare provider about all of your medical conditions, including if you:

- have heart problems
- have bleeding problems
- have or have had ulcers
- have liver or kidney problems
- have high blood pressure
- have asthma
- are pregnant or plan to become pregnant. Taking mefenamic acid capsules at about 20 weeks of pregnancy or later may harm your unborn baby.
  - If you need to take mefenamic acid capsules 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 mefenamic acid capsules after about 30 weeks of pregnancy.**
  - Mefenamic acid capsules may cause fertility problems in females, which may affect your ability to become pregnant. Talk to your healthcare provider if this is a concern for you.
- are breastfeeding or plan to breastfeed. Mefenamic acid can pass into your breast milk. Talk to your healthcare provider about the best way to feed your baby during treatment with mefenamic acid capsules.

Tell your healthcare provider about all of the medicines you take, including prescription or over-the-counter medicines, vitamins, or herbal supplements. Mefenamic acid capsules 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.**

How should I take mefenamic acid capsules?

- Take mefenamic acid capsules exactly as your healthcare provider tells you to take it.

If you take too much mefenamic acid capsules, call your healthcare provider or Poison Help Line at 1-800-222-1222, or go to the nearest hospital emergency room right away.

What are the possible side effects of mefenamic acid capsules?

Mefenamic acid capsules may cause serious side effects, including:

See "What is the most important information I should know about mefenamic acid capsules, and medicines called nonsteroidal anti-inflammatory drugs (NSAIDs)?"

- liver problems including liver failure
- new or worse high blood pressure
- heart failure
- kidney problem including kidney failure
- increase in blood potassium level (hyperkalemia)
- life-threatening allergic reactions
- asthma attacks in people who have asthma
- serious skin reactions, including life-threatening skin reactions
- low red blood cells (anemia)

Other side effects of mefenamic acid capsules include: stomach pain, constipation, diarrhea, indigestion, gas, heartburn, nausea, vomiting, dizziness, swelling, increased liver enzyme levels, headaches, itching, rashes, and ringing in the ear.

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

- shortness of breath or trouble breathing
- chest pain
- weakness in one part or side of your body
- slurred speech
- swelling of the face or throat

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

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

These are not all of the possible side effects of mefenamic acid capsules.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or Lupin Pharmaceuticals, Inc at 1-800-399-2561.

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.

How should I store mefenamic acid capsules?

- Store mefenamic acid capsules at room temperature at 25°C (77°F).

Keep mefenamic acid capsules and all medicines out of the reach of children.

General information about the safe and effective use of mefenamic acid capsules.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use mefenamic acid capsules for a condition for which it was not prescribed. Do not give mefenamic acid capsules to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about mefenamic acid capsules that is written for health professionals.

What are the ingredients in mefenamic acid capsules?
Active ingredient: mefenamic acid
Inactive ingredient: lactose monohydrate and magnesium stearate. The capsule shell contains gelatin, sodium lauryl sulfate, titanium dioxide, D&C yellow No. 10, FD&C yellow No. 6 and FD&C red No. 3.

Manufactured for:
Lupin Pharmaceuticals, Inc.
Naples, FL 34108
United States

Manufactured by:
Lupin Limited
Goa 403 722
INDIA

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Revised: 02/2026 ID: 282952