

MECLOFENAMATE SODIUM- meclufenamate sodium capsule
Mylan Pharmaceuticals Inc.

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).
- Meclofenamate sodium capsules are contraindicated in the setting of coronary artery bypass graft (CABG) surgery (see CONTRAINDICATIONS and WARNINGS).

Gastrointestinal Risk

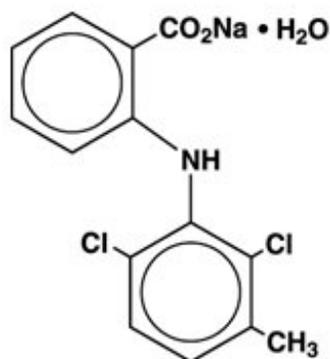
- NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal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

DESCRIPTION

Meclofenamate sodium is N-(2,6-dichloro-m-tolyl) anthranilic acid, sodium salt, monohydrate. It is an anti-inflammatory drug for oral administration. Meclofenamate sodium capsules, USP contain 50 mg or 100 mg meclufenamic acid as the sodium salt and the following inactive ingredients: colloidal silicon dioxide, D&C Yellow No. 10, FD&C Blue No. 1, FD&C Red No. 3, gelatin, magnesium stearate, microcrystalline cellulose, pregelatinized starch (corn), sodium lauryl sulfate and titanium dioxide.

In addition, the imprinting ink contains black iron oxide, D&C Yellow No. 10 Aluminum Lake, FD&C Blue No. 1 Aluminum Lake, FD&C Blue No. 2 Aluminum Lake, FD&C Red No. 40 Aluminum Lake, propylene glycol and shellac glaze.

The structural formula of meclufenamate sodium is:



Molecular Formula: C₁₄H₁₀Cl₂NNaO₂•H₂O

It is a white to creamy white, odorless to almost odorless, crystalline powder with melting point 287° to 291°C, molecular weight 336.15, and it is freely soluble in water.

CLINICAL PHARMACOLOGY

Pharmacodynamics

Meclofenamate sodium is a nonsteroidal agent which has demonstrated anti-inflammatory, analgesic, and antipyretic activity in laboratory animals. The mode of action, like that of other nonsteroidal anti-inflammatory agents, is not known. Therapeutic action does not result from pituitary-adrenal stimulation. In animal studies, meclofenamate sodium was found to inhibit prostaglandin synthesis and to compete for binding at the prostaglandin receptor site. *In vitro*, meclofenamate sodium was found to be an inhibitor of human leukocyte 5-lipoxygenase activity. These properties may be responsible for the anti-inflammatory action of meclofenamate sodium. There is no evidence that meclofenamate sodium alters the course of the underlying disease.

In several human isotope studies, meclofenamate sodium, at a dosage of 300 mg/day, produced a fecal blood loss of 1 to 2 mL per day, and 2 to 3 mL per day at 400 mg/day. Aspirin, at a dosage of 3.6 g/day, caused a fecal blood loss of 6 mL per day.

In a multiple-dose, 1-week study in normal human volunteers, meclofenamate sodium had little or no effect on collagen-induced platelet aggregation, platelet count, or bleeding time. In comparison, aspirin suppressed collagen-induced platelet aggregation and increased bleeding time. The concomitant administration of antacids (aluminum and magnesium hydroxides) does not interfere with absorption of meclofenamate sodium.

Pharmacokinetics

Meclofenamate sodium is rapidly absorbed in man following single and multiple oral doses with peak plasma concentrations occurring in 0.5 to 2 hours. Based on a comparison to a suspension of meclofenamic acid, meclofenamate sodium is completely bioavailable.

The plasma concentrations of meclofenamic acid decline monoexponentially following oral administration. In a study in ten healthy subjects following a single oral dose the apparent elimination half-life ranged from 0.8 to 5.3 hours. After the administration of meclofenamate sodium for 14 days every 8 hours, the apparent elimination half-life ranged from 0.8 to 2.1 hours with no evidence of accumulation of meclofenamic acid in plasma (see Table).

TABLE SUMMARY OF MECLOFENAMATE SODIUM PHARMACOKINETIC PARAMETERS

Mean (Range) Parameter Values (n = 10)		
	Meclofenamic Acid 100 mg*	Metabolite I [†]
C _{max} mcg/mL [‡]	4.8 (1.8 to 7.2)	1 (0.5 to 1.5)

t_{max} hr [§]	0.9 (0.5 to 1.5)	2.4 (0.5 to 4)
C_{min} mcg/mL [¶]	0.2 (0.5 to 1.5)	0.4 (0.2 to 1.1)
Cl/F mL/min [#]	206 (126 to 342)	---
Vd/F liters ^p	23.3 (9.1 to 43.2)	---
$t_{1/2}$ hr ^β	1.3 (0.8 to 2.1)	15.3 ^à
% of Dose in Urine Unconjugated	0 ---	0.5 (0 to 1.2)
Total	2.7 (0 to 4.5)	21.6 (7.5 to 32.6)

* Administered every 8 hours for 14 days

† 3-Hydroxymethyl metabolite of meclofenamic acid with 20% activity of meclofenamate sodium *in vitro*

‡ Peak plasma concentration

§ Time to peak plasma concentration

¶ Trough plasma concentration

Oral clearance

p Oral distribution volume

β Elimination half-life

à Estimated from mean data

Meclofenamic acid is extensively metabolized to an active metabolite (Metabolite I; 3-hydroxymethyl metabolite of meclofenamic acid) and at least six other less well characterized minor metabolites. Only this Metabolite I has been shown *in vitro* to inhibit cyclooxygenase activity with approximately one fifth the activity of meclofenamate sodium. Metabolite I (3-hydroxymethyl metabolite of meclofenamic acid) with a mean half-life of approximately 15 hours did accumulate following multiple dosing. After the administration of 100 mg meclofenamate sodium for 14 days every 8 hours, Metabolite I reached a peak plasma concentration of only 1 mcg/mL. By contrast, the peak concentration was 4.8 mcg/mL for the parent compound on both days 1 and 14. Therefore, the accumulation of Metabolite I is probably not clinically significant.

Approximately 70% of the administered dose is excreted by the kidneys with 8% to 35% excreted as predominantly conjugated species of meclofenamic acid and Metabolite I (see Table). Other metabolites, whose excretion rates are unknown, account for the remaining 35% to 62% of the dose excreted in the urine. The remainder of the administered dose (approximately 30%) is eliminated in the feces (apparently through biliary excretion). There is insufficient experience to know if meclofenamate sodium or its metabolites accumulate in patients with compromised renal or hepatic function. Therefore, meclofenamate sodium should be used with caution in these patients (see PRECAUTIONS). Trace amounts of meclofenamate sodium are excreted in human breast milk.

Meclofenamic acid is greater than 99% bound to plasma proteins over a wide drug concentration range.

Unlike most NSAIDs, which when administered with food have a decrease in rate but not in extent of absorption, meclofenamic acid is decreased in both. It has been reported that following the administration of meclofenamate sodium capsules one-half hour after a meal, the average extent of bioavailability decreased by 26%, the average peak concentration (C_{max}) decreased 4-fold and the time to C_{max} was delayed by 3 hours.

Clinical Studies

Controlled clinical trials comparing meclofenamate sodium with aspirin demonstrated comparable efficacy in rheumatoid arthritis.

The meclofenamate sodium treated patients had fewer reactions involving the special senses, specifically tinnitus, but more gastrointestinal reactions, specifically diarrhea.

The incidence of patients who discontinued therapy due to adverse reactions was similar for both the meclofenamate sodium and aspirin-treated groups.

The improvement with meclofenamate sodium reported by patients and the reduction of the disease activity as evaluated by both physicians and patients with rheumatoid arthritis are associated with a significant reduction in number of tender joints, severity of tenderness, and duration of morning stiffness.

The improvement reported by patients and as evaluated by physicians in patients treated with meclofenamate sodium for osteoarthritis is associated with a significant reduction in night pain, pain on walking, degree of starting pain, and pain on passive motion. The function of knee joints also improved significantly.

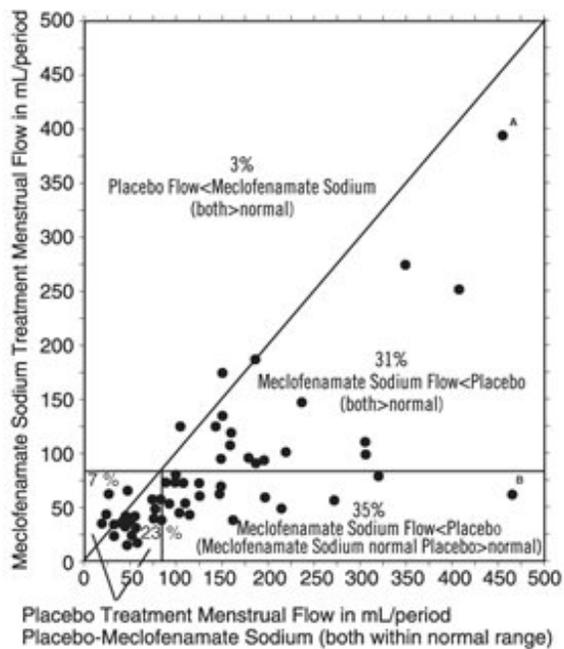
Meclofenamate sodium has been used in combination with gold salts or corticosteroids in patients with rheumatoid arthritis. Studies have demonstrated that meclofenamate sodium contributes to the improvement of patients' conditions while maintained on gold salts or corticosteroids. Data are inadequate to demonstrate that meclofenamate sodium in combination with salicylates produces greater improvement than that achieved with meclofenamate sodium alone.

In controlled clinical trials of patients with mild to moderate pain, meclofenamate sodium 50 mg provided significant pain relief. In these studies of episiotomy and dental pain, meclofenamate sodium 100 mg demonstrated additional benefit in some patients. The onset of analgesic effect was generally within one hour and the duration of action was 4 to 6 hours.

In controlled clinical trials of patients with dysmenorrhea, meclofenamate sodium 100 mg t.i.d. provided significant reduction in the symptoms associated with dysmenorrhea.

In randomized double-blind crossover trials of meclofenamate sodium 100 mg t.i.d. versus placebo in women with heavy menstrual blood loss (MBL), meclofenamate sodium treatment was usually associated with a reduction in menstrual flow.

The graph below is a scatter plot of menstrual flow from the average of two menstrual periods on meclofenamate sodium treatments (vertical axis) versus two menstrual periods on placebo (horizontal axis) for 55 women. Of note, although the amount of reduction in MBL was variable, some degree of reduction occurred in 90% of women in this study.



Scattergram of Menstrual Flow Average of Two Periods on Each Treatment of 55 Women from Three Clinical Trials

The points on the graph represent the mean MBL for each subject when treated for two periods with placebo and two periods with meclufenamate sodium. To ease in interpretation, the following examples may be helpful. Point A represents a woman who had MBL of 459 mL while on placebo, and 405 mL on meclufenamate sodium. Point B represents a woman who had MBL of 472 mL while on placebo, and 64 mL when treated with meclufenamate sodium.

In association with this reduction in menstrual blood loss, the duration of menses was decreased by one day; tampon/pad usage was decreased by an average of two per day on the 2 days of heaviest flow; and symptoms of dysmenorrhea were significantly reduced.

INDICATIONS AND USAGE

Carefully consider the potential benefits and risks of meclufenamate sodium capsules and other treatment options before deciding to use meclufenamate sodium capsules. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see WARNINGS).

Meclofenamate sodium capsules are indicated:

- For reduction of fever in adults
- For relief of mild to moderate pain in adults
- For relief of signs and symptoms of juvenile arthritis.
- For relief of the signs and symptoms of rheumatoid arthritis
- For relief of the signs and symptoms of osteoarthritis.
- For treatment of primary dysmenorrhea.
- For acute or long-term use in the relief of signs and symptoms of the following:

1. Ankylosing spondylitis

2. Acute painful shoulder (Acute subacromial bursitis/supraspinatus tendinitis)
3. Acute gouty arthritis

Meclofenamate sodium capsules are also indicated for the treatment of idiopathic heavy menstrual blood loss (see CLINICAL PHARMACOLOGY and PRECAUTIONS).

As with all nonsteroidal anti-inflammatory drugs, selection of meclufenamate sodium capsules require a careful assessment of the benefit/risk ratio (see WARNINGS, PRECAUTIONS and ADVERSE REACTIONS).

Meclofenamate sodium capsules are not recommended in children because adequate studies to demonstrate safety and efficacy have not been carried out.

CONTRAINDICATIONS

Meclofenamate sodium capsules are contraindicated in patients with known hypersensitivity to meclufenamate sodium.

Meclofenamate sodium capsules should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients (see WARNINGS: Anaphylactoid Reactions and PRECAUTIONS: Preexisting Asthma).

Meclofenamate sodium capsules are contraindicated in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).

WARNINGS

Cardiovascular Effects

Cardiovascular Thrombotic Events

Clinical trials of several COX-2 selective and nonselective NSAIDs of up to 3 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 meclufenamate sodium, increases the risk of serious gastrointestinal (GI) events (see WARNINGS).

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 4 years of follow-up.

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

Hypertension

NSAIDs, including meclufenamate sodium, can lead to onset of new hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including meclufenamate sodium, should be used with caution in patients with hypertension. Blood pressure (BP) should be monitored closely 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 2-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 meclufenamate sodium 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).

Avoid the use of meclufenamate sodium capsules in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If meclufenamate sodium capsules are used in patients with severe heart failure, monitor

patients for signs of worsening heart failure.

Gastrointestinal Effects

Risk of Ulceration, Bleeding, and Perforation

NSAIDs, including meclufenamate sodium, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the 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. These trends continue with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.

NSAIDs should be prescribed with extreme caution in those with a prior history of ulcer disease or gastrointestinal bleeding. Patients with a *prior history of peptic ulcer disease and/or gastrointestinal bleeding* who use NSAIDs have a greater than 10-fold increased risk for developing a GI bleed compared to patients with neither of these risk factors. Other factors that increase the risk for GI bleeding in patients treated with NSAIDs include concomitant use of oral corticosteroids or anticoagulants, longer duration of NSAID therapy, smoking, use of alcohol, older age, and poor general health status. Most spontaneous reports of fatal GI events are in elderly or debilitated patients and therefore, special care should be taken in treating this population.

To minimize the potential risk for an adverse GI event in patients treated with an NSAID, the lowest effective dose should be used for the shortest possible duration. Patients and physicians should remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy and promptly initiate additional evaluation and treatment if a serious GI adverse event is suspected. This should include discontinuation of the NSAID until a serious GI adverse event is ruled out. For high risk patients, alternate therapies that do not involve NSAIDs should be considered.

Renal Effects

Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of a nonsteroidal anti-inflammatory drug may cause a dose dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.

Advanced Renal Disease

No information is available from controlled clinical studies regarding the use of meclufenamate sodium in patients with advanced renal disease. Therefore, treatment with meclufenamate sodium is not recommended in these patients with advanced renal

disease. If meclofenamate sodium therapy must be initiated, close monitoring of the patient's renal function is advisable.

Anaphylactoid Reactions

As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to meclofenamate sodium. Meclofenamate sodium should not be given to patients with the aspirin triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs (see CONTRAINDICATIONS and PRECAUTIONS: Preexisting Asthma). Emergency help should be sought in cases where an anaphylactoid reaction occurs.

Skin Reactions

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

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 meclofenamate sodium capsules. 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 meclofenamate sodium capsules and evaluate the patient immediately.

Fetal Toxicity

Premature Closure of Fetal Ductus Arteriosus

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

Oligohydramnios/Neonatal Renal Impairment

Use of NSAIDs, including meclofenamate sodium capsules, 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 meclufenamate sodium capsules use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if meclufenamate sodium capsules treatment extends beyond 48 hours. Discontinue meclufenamate sodium capsules if oligohydramnios occurs and follow up according to clinical practice (see PRECAUTIONS: Pregnancy).

PRECAUTIONS

General

Meclofenamate sodium 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.

The pharmacological activity of meclufenamate sodium in reducing fever and inflammation may diminish the utility of these diagnostic signs in detecting complications of presumed noninfectious, painful conditions.

Hepatic Effects

Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs including meclufenamate sodium. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continuing therapy. Notable elevations of ALT or AST (approximately 3 or more times the upper limit of normal) have been reported in approximately 1% of patients in clinical trials with NSAIDs. In addition, rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis and hepatic failure, some of them with fatal outcomes have been reported.

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

Hematological Effects

Anemia is sometimes seen in patients receiving NSAIDs, including meclufenamate sodium. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including meclufenamate sodium, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia.

NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of

shorter duration, and reversible. Patients receiving meclufenamate sodium who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants, should be carefully monitored.

Preexisting Asthma

Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs has been reported in such aspirin-sensitive patients, meclufenamate sodium should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma.

Information for Patients

Patients should be informed of the following information before initiating therapy with an NSAID and periodically during the course of ongoing therapy. Patients should also be encouraged to read the NSAID Medication Guide that accompanies each prescription dispensed.

1. **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).
2. Meclufenamate sodium, like other NSAIDs, can cause GI discomfort and, rarely, serious GI side effects, such as ulcers and bleeding, which may result in hospitalization and even death. Although serious GI tract ulcerations and bleeding can occur without warning symptoms, patients should be alert for the signs and symptoms of ulcerations and bleeding, and should ask for medical advice when observing any indicative sign or symptoms including epigastric pain, dyspepsia, melena, and hematemesis. Patients should be apprised of the importance of this follow-up (see **WARNINGS: Gastrointestinal Effects: Risk of Ulceration, Bleeding, and Perforation**).
3. **Serious Skin Reactions, including DRESS:** Advise patients to stop taking meclufenamate sodium capsules immediately if they develop any type of rash or fever and to contact their healthcare provider as soon as possible (see WARNINGS).
4. **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).
5. Patients should be informed of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, pruritus, jaundice, right upper quadrant tenderness, and “flu-like” symptoms). If these occur, patients should be instructed to stop therapy and seek immediate medical therapy.
6. Patients should be informed of the signs of an anaphylactoid reaction (e.g., difficulty breathing, swelling of the face or throat). If these occur, patients should be instructed to seek immediate emergency help (see WARNINGS).
7. **Fetal Toxicity:** Inform pregnant women to avoid use of meclufenamate sodium 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

meclofenamate sodium 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: Fetal Toxicity, PRECAUTIONS: Pregnancy).

Laboratory Tests

Because serious GI tract ulcerations and bleeding can occur without warning symptoms, physicians should monitor for signs or symptoms of GI bleeding. Patients on long-term treatment with NSAIDs, should have their CBC and a chemistry profile checked periodically. If clinical signs and symptoms consistent with liver or renal disease develop, systemic manifestations occur (e.g., eosinophilia, rash, etc.) or if abnormal liver tests persist or worsen, meclufenamate sodium should be discontinued.

Drug Interactions

ACE-inhibitors

Reports suggest that NSAIDs may diminish the antihypertensive effect of ACE-inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE-inhibitors.

Aspirin

When meclufenamate sodium is administered with aspirin, its protein binding is reduced, although the clearance of free meclufenamate sodium is not altered. The clinical significance of this interaction is not known; however, as with other NSAIDs, concomitant administration of meclufenamate sodium capsules and aspirin is not generally recommended because of the potential of increased adverse effects.

Furosemide

Clinical studies, as well as post-marketing observations, have shown that meclufenamate sodium can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, the patient should be observed closely for signs of renal failure (see PRECAUTIONS: Renal Effects), as well as to assure diuretic efficacy.

Lithium

NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs of lithium toxicity.

Methotrexate

NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This may indicate that they could enhance the toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.

Warfarin

The effects of warfarin and NSAIDs on GI bleeding are synergistic, such that users of both drugs together have a risk of serious GI bleeding higher than users of either drug alone.

Carcinogenesis

An 18-month study in rats revealed no evidence of carcinogenicity.

Pregnancy

Risk Summary

Use of NSAIDs, including meclofenamate sodium capsules, 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 meclofenamate sodium capsules use between about 20 and 30 weeks of gestation, and avoid meclofenamate sodium capsules 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 meclofenamate sodium capsules, 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. Animal reproductive studies conducted in rats and rabbits have not demonstrated evidence of developmental abnormalities. However, animal reproduction studies are not always predictive of human response. 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 meclofenamate, 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 2-4% and 15-20%, 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 meclufenamate sodium capsules, 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 meclufenamate sodium capsules treatment extends beyond 48 hours, consider monitoring with ultrasound for oligohydramnios. If oligohydramnios occurs, discontinue meclufenamate sodium capsules 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 neonatal renal dysfunction required treatment with invasive procedures, 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.

Labor and Delivery

In rat studies with NSAIDs, as with other drugs known to inhibit prostaglandin synthesis, an increased incidence of dystocia, delayed parturition, and decreased pup survival occurred. The effects of meclufenamate sodium on labor and delivery in pregnant

women are unknown.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human-milk and because of the potential for serious adverse reactions in nursing infants from meclofenamate sodium, 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.

Pediatric Use

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

Geriatric Use

As with any NSAIDs, caution should be exercised in treating the elderly (65 years and older).

ADVERSE REACTIONS

Incidence Greater Than 1%

The following adverse reactions were observed in clinical trials and included observations from more than 2,700 patients, 594 of whom were treated for one year and 248 for at least 2 years.

Gastrointestinal

The most frequently reported adverse reactions associated with meclofenamate sodium involve the gastrointestinal system. In controlled studies of up to 6 months duration, these disturbances occurred in the following decreasing order of frequency with the approximate incidences in parentheses: diarrhea (10% to 33%), nausea with or without vomiting (11%), other gastrointestinal disorders (10%), and abdominal pain*. In long-term uncontrolled studies of up to 4 years duration, one third of the patients had at least one episode of diarrhea some time during meclofenamate sodium therapy.

In approximately 4% of the patients in controlled studies, diarrhea was severe enough to require discontinuation of meclofenamate sodium. The occurrence of diarrhea is dose related, generally subsides with dose reduction, and clears with termination of therapy. The incidence of diarrhea in patients with osteoarthritis is generally lower than that reported in patients with rheumatoid arthritis.

Other reactions less frequently reported were pyrosis*, flatulence*, anorexia, constipation, stomatitis, and peptic ulcer. The majority of the patients with peptic ulcer had either a history of ulcer disease or were receiving concomitant anti-inflammatory drugs, including corticosteroids which are known to produce peptic ulceration.

Cardiovascular: edema

Dermatologic: rash*, urticaria, pruritus

Central Nervous System: headache*, dizziness*

Special Senses: tinnitus

* Incidence between 3% and 9%. Those reactions occurring in 1% to 3% of patients are not marked with an asterisk.

Incidence Less Than 1%—Probably Causally Related

The following adverse reactions were reported less frequently than 1% during controlled clinical trials and through voluntary reports since marketing. The probability of a causal relationship exists between the drug and these adverse reactions.

Gastrointestinal: bleeding and/or perforation with or without obvious ulcer formation, colitis, cholestatic jaundice

Renal: renal failure

Hematologic: neutropenia, thrombocytopenic purpura, leukopenia, agranulocytosis, hemolytic anemia, eosinophilia, decrease in hemoglobin and/or hematocrit

Dermatologic: erythema multiforme, Stevens-Johnson Syndrome, exfoliative dermatitis

Hepatic: alteration of liver function tests

Allergic: lupus and serum sickness-like symptoms

Incidence Less Than 1%—Causal Relationship Unknown

Other reactions have been reported but under conditions where a causal relationship could not be established. However, in these rarely reported events, that possibility cannot be excluded. Therefore, these observations are listed to alert physicians.

Cardiovascular: palpitations

Central Nervous System: malaise, fatigue, paresthesia, insomnia, depression

Special Senses: blurred vision, taste disturbances, decreased visual acuity, temporary loss of vision, reversible loss of color vision, retinal changes including macular fibrosis, macular and perimacular edema, conjunctivitis, iritis

Renal: nocturia

Gastrointestinal: paralytic ileus

Dermatologic: erythema nodosum, hair loss

OVERDOSAGE

The following is based on the little information available concerning overdosage with meclofenamate sodium and related compounds. After a massive overdose, CNS stimulation may be manifested by irrational behavior, marked agitation and generalized seizures. Following this phase, renal toxicity (falling urine output, rising creatinine, abnormal urinary cellular elements) may be noted with possible oliguria or anuria and azotemia. A 24 year-old male was anuric for approximately one week after ingesting an overdose of 6 to 7 grams of meclofenamate sodium. Spontaneous diuresis and recovery subsequently occurred.

Management consists of emptying the stomach by emesis or lavage and instilling an

ample dose of activated charcoal into the stomach. There is some evidence that charcoal will actively absorb meclufenamate sodium, but dialysis or hemoperfusion may be less effective because of plasma protein binding. The seizures should be controlled by an appropriate anticonvulsant regimen. Attention should be directed throughout, by careful monitoring, to the preservation of vital functions and fluid-electrolyte balance. Dialysis may be required to correct serious azotemia or electrolyte imbalance.

DOSAGE AND ADMINISTRATION

Carefully consider the potential benefits and risks of meclufenamate sodium capsules and other treatment options before deciding to use meclufenamate sodium capsules. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see WARNINGS).

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

Usual Dosage

For Mild to Moderate Pain

The recommended dose is 50 mg every 4 to 6 hours. Doses of 100 mg may be needed in some patients for optimal pain relief (see CLINICAL PHARMACOLOGY). However, the daily dose should not exceed 400 mg (see ADVERSE REACTIONS).

For excessive menstrual blood loss and primary dysmenorrhea

The recommended dose of meclufenamate sodium is 100 mg 3 times a day, for up to 6 days, starting at the onset of menstrual flow.

For rheumatoid arthritis and osteoarthritis (including acute exacerbations of chronic disease)

The dosage is 200 mg to 400 mg per day, administered in three or four equal doses.

Therapy should be initiated at the lower dosage, then increased as necessary to improve clinical response. The dosage should be individually adjusted for each patient, depending on the severity of the symptoms and the clinical response. The daily dosage should not exceed 400 mg per day. The smallest dosage of meclufenamate sodium that yields clinical control should be employed.

Although improvement may be seen in some patients in a few days, 2 to 3 weeks of treatment may be required to obtain the optimum therapeutic benefit.

After a satisfactory response has been achieved, the dosage should be adjusted as required. A lower dosage may suffice for long-term administration.

If gastrointestinal complaints occur (see WARNINGS and PRECAUTIONS), meclufenamate sodium may be administered with meals or with milk (see CLINICAL PHARMACOLOGY for a description of food effects). If intolerance occurs, the dosage may need to be reduced. Therapy should be terminated if any severe adverse reactions occur.

HOW SUPPLIED

Meclofenamate Sodium Capsules, USP are available containing either 50 mg or 100 mg of meclufenamic acid as the sodium salt.

The 50 mg capsules are hard-shell gelatin capsules with a coral opaque cap and a coral opaque body filled with an off-white powder blend. The capsules are axially printed with **MYLAN** over **2150** in black ink on both the cap and body. They are available as follows:

NDC 0378-2150-01
bottles of 100 capsules

The 100 mg capsules are hard-shell gelatin capsules with a coral opaque cap and a white opaque body filled with an off-white powder blend. The capsules are axially printed with **MYLAN** over **3000** in black ink on both the cap and body. They are available as follows:

NDC 0378-3000-01
bottles of 100 capsules

Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

Protect from light and moisture.

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.

PHARMACIST: Dispense a Medication Guide with each prescription.

Medication Guide for Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

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

NSAIDs can 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:
 - o with increasing doses of NSAIDs
 - o 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.

- **Increased risk of bleeding, ulcers, and tears (perforation) of the esophagus (tube leading from the mouth to the stomach), stomach and intestines:**
 - o anytime during use
 - o without warning symptoms
 - o that may cause death

The risk of getting an ulcer or bleeding increases with:

- o past history of stomach ulcers, or stomach or intestinal bleeding with use of NSAIDs
- o taking medicines called “corticosteroids”, “anticoagulants”, “SSRIs”, or “SNRIs”

- | | |
|------------------------------|--------------------------|
| o increasing doses of NSAIDs | o older age |
| o longer use of NSAIDs | o poor health |
| o smoking | o advanced liver disease |
| o drinking alcohol | o bleeding problems |

NSAIDs should only be used:

- o exactly as prescribed
- o at the lowest dose possible for your treatment
- o for 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 your 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 breast feed.

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 problems including kidney failure
- low red blood cells (anemia)
- life-threatening skin reactions
- life threatening allergic reactions
- **Other side effects of 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
- chest pain
- weakness in one part or side of your body
- slurred speech
- swelling of the face or throat

Stop taking your NSAID 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 your 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

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

These are not all 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 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 NSAIDs 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 they were not prescribed. Do not give NSAIDs to other people, even if they have the same symptoms that you have. They 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.

Manufactured for: Mylan Pharmaceuticals Inc., Morgantown, WV 26505 U.S.A.
For more information, call Mylan at 1-877-446-3679 (1-877-4-INFO-RX).

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

Manufactured for:

Mylan Pharmaceuticals Inc.
Morgantown, WV 26505 U.S.A.

Manufactured by:

Mylan Laboratories Limited
Hyderabad — 500 096, India

75079821

Revised: 5/2021

MX:MCFT:R3m/MX:MG:MCFT:R2m

PRINCIPAL DISPLAY PANEL - 50 mg

NDC 0378-2150-01

**Meclofenamate
Sodium
Capsules, USP
50 mg**

**PHARMACIST: Dispense the accompanying
Medication Guide to each patient.**

Rx only 100 Capsules

Each capsule contains:

Meclofenamate sodium, USP monohydrate
equivalent to 50 mg of meclofenamate acid.

Usual Dosage: 200 mg to 400 mg per day;
administered in three or four equal doses.

See package insert for full prescribing
information.

**Keep this and all medication out of
the reach of children.**

**Store at 20° to 25°C (68° to 77°F). [See
USP Controlled Room Temperature.]**

Protect from light and moisture.

Manufactured for:

Mylan Pharmaceuticals Inc.

Morgantown, WV 26505 U.S.A.

Made in India

Mylan.com

RMX2150A

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.

Keep container tightly closed.

Code No.: MH/DRUGS/25/NKD/89

Each capsule contains:
Meclofenamate sodium, USP monohydrate equivalent to 50 mg of meclofenamate acid.
Usual Dosage: 200 mg to 400 mg per day; administered in three or four equal doses. See package insert for full prescribing information.
Keep this and all medication out of the reach of children.
Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]
Protect from light and moisture.
Manufactured for:
Mylan Pharmaceuticals Inc.
Morgantown, WV 26505 U.S.A.
Made in India

NDC 0378-2150-01

Meclofenamate Sodium Capsules, USP

50 mg

PHARMACIST: Dispense the accompanying Medication Guide to each patient.

Rx only **100 Capsules**

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure. Keep container tightly closed.
Code No.: MH/DRUGS/25/NKD/89

(40 x 15 mm)
Varnish Free area for Variable Data Coding

GTIN XXXXXXXXXXXXXXXX
S/N XXXXXXXXXXXX
EXP MM YYYY
LOT XXXXXXXX

PRINCIPAL DISPLAY PANEL - 100 mg

NDC 0378-3000-01

Meclofenamate Sodium Capsules, USP
100 mg

PHARMACIST: Dispense the accompanying Medication Guide to each patient.

Rx only 100 Capsules

Each capsule contains:
Meclofenamate sodium, USP monohydrate equivalent to 100 mg of meclofenamate acid.

Usual Dosage: 200 mg to 400 mg per day; administered in three or four equal doses.

See package insert for full prescribing information.

Keep this and all medication out of the reach of children.

Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

Protect from light and moisture.

Manufactured for:
Mylan Pharmaceuticals Inc.
Morgantown, WV 26505 U.S.A.

Made in India

Mylan.com

RMX3000A

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.

Keep container tightly closed.

Code No.: MH/DRUGS/25/NKD/89

Each capsule contains:
Meclofenamate sodium, USP monohydrate equivalent to 100 mg of meclofenamate acid.
Usual Dosage: 200 mg to 400 mg per day; administered in three or four equal doses. See package insert for full prescribing information.
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Protect from light and moisture.
Manufactured for:
Mylan Pharmaceuticals Inc.
Morgantown, WV 26505 U.S.A.
Made in India

NDC 0378-3000-01

Meclofenamate Sodium Capsules, USP

100 mg

PHARMACIST: Dispense the accompanying Medication Guide to each patient.

Mylan®

Rx only 100 Capsules

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure. Keep container tightly closed.
Code No.: MH/DRUGS/25/NKD/89

(40 x 15 mm)
Varnish Free area for Variable Data Coding

75070361

GTIN XXXXXXXXXXXXX
S/N XXXXXXXXXXXX
EXP MM YYYY
LOT XXXXXXXX

MECLOFENAMATE SODIUM

meclofenamate sodium capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0378-2150
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
MECLOFENAMATE SODIUM (UNII: 94NJ818U2W) (MECLOFENAMIC ACID - UNII:48I5LU4ZWD)	MECLOFENAMIC ACID	50 mg

Inactive Ingredients

Ingredient Name	Strength
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C RED NO. 3 (UNII: PN2ZH5LOQY)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
STARCH, CORN (UNII: O8232NY3SJ)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERROSO FERRIC OXIDE (UNII: XM0M87F357)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SHELLAC (UNII: 46N107B71O)	

Product Characteristics

Color	PINK (coral opaque)	Score	no score
Shape	CAPSULE	Size	14mm
Flavor		Imprint Code	MYLAN;2150
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0378-2150-01	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	09/03/1986	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA071081	09/03/1986	

MECLOFENAMATE SODIUM

meclofenamate sodium capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0378-3000
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
MECLOFENAMATE SODIUM (UNII: 94NJ818U2W) (MECLOFENAMIC ACID - UNII:48I5LU4ZWD)	MECLOFENAMIC ACID	100 mg

Inactive Ingredients

Ingredient Name	Strength
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C RED NO. 3 (UNII: PN2ZH5LOQY)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
STARCH, CORN (UNII: O8232NY3SJ)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERROSFERRIC OXIDE (UNII: XM0M87F357)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SHELLAC (UNII: 46N107B71O)	

Product Characteristics

Color	PINK (coral opaque) , WHITE (white opaque)	Score	no score
Shape	CAPSULE	Size	15mm
Flavor		Imprint Code	MYLAN;3000
Contains			

Packaging

#	Item Code	Package Description	Marketing Start	Marketing End
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#	Item Code	Package Description	Date	Date
1	NDC:0378-3000-01	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	09/03/1986	
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
ANDA	ANDA071081	09/03/1986		

Labeler - Mylan Pharmaceuticals Inc. (059295980)

Revised: 5/2021

Mylan Pharmaceuticals Inc.