

MELOXICAM meloxicam tablet
Opiurna Inc.
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BRIEF SUMMARY OF PRESCRIBING INFORMATION

This highlights do not include all the information needed to use Meloxicam Tablets USP safely and effectively. See full prescribing information for Meloxicam Tablets USP.

Meloxicam Tablets USP, for oral use
Indicated US Approval: 2004

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS
See full prescribing information for complete brief summary.

- **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 (5.1).
- Meloxicam tablets are contraindicated in the setting of coronary artery bypass graft (CABG) surgery (4.3).
- 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 upper GI bleeding are at greater risk for serious GI events (5.2).

Recent Warnings 2018:
Interaction and Danger: Acute Respiratory Distress Syndrome (ARDS) in patients with Polycystic Ovary Syndrome (PCOS) (1.3) (2.0);
Design and Administration, Care of Dosing Instructions (2.1) (2.0);
Design and Administration, Juvenile Rheumatoid Arthritis (JRA) Pauciarticular and Polyarticular Course (2.4) (2.0);
Warnings and Precautions, Cardiovascular Thrombotic Events (5.1) (2.0)

INDICATIONS AND USAGE
Meloxicam tablets are a non-steroidal anti-inflammatory drug indicated for:

- Osteoarthritis (OA) (1.1)
- Rheumatoid Arthritis (RA) (1.2)
- Juvenile Rheumatoid Arthritis (JRA) in patients who weigh ≥60 kg (1.3)

DOSE AND ADMINISTRATION
Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals (2.1)

- OA (2.1) and RA (2.1):
Starting dose: 7.5 mg once daily
Dose may be increased to 15 mg once daily
- JRA (2.4)
- 7.5 mg once daily in children ≥60 kg

Meloxicam Tablets are not interchangeable with approved formulations of meloxicam even if the total milligram strength is the same (2.6)

DOSE FORM AND STRENGTH

- Meloxicam Tablets USP 7.5 mg and 15 mg (2)

CONTRAINDICATIONS

- Known hypersensitivity to meloxicam or any component of the drug product (4)
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs (4)
- In the setting of CABG surgery (4)

WARNINGS AND PRECAUTIONS

- **Warnings:** Inform patients of warning signs and symptoms of hepatotoxicity. Discontinue if abnormal liver test results occur (5.3).
Precautions: Inform patients of non-steroidal anti-inflammatory drug (NSAID) risks including cardiovascular (CV) thrombotic events, ulcers and bleeding (5.1, 5.2).
Information to Patients: Do not use Meloxicam Tablets USP if you are pregnant or may become pregnant during treatment (5.4).
Cardiovascular Thrombotic Events: In the setting of CABG surgery, do not use Meloxicam Tablets USP (4.3).
Respiratory Events: Monitor respiratory symptoms in patients with asthma or history of respiratory tract disease. Advise patients to stop taking Meloxicam Tablets USP if they experience asthma symptoms (5.5).
Renal Impairment: Monitor renal function in patients with advanced renal disease. Advise patients to stop taking Meloxicam Tablets USP if they experience renal symptoms (5.6).
Use in Children: Monitor for signs and symptoms of anemia in patients with iron deficiency (5.7).
Use in Pregnancy: Advise patients to stop taking Meloxicam Tablets USP if they become pregnant (5.4).
Use in Nursing Women: Advise patients to avoid breastfeeding while taking Meloxicam Tablets USP (5.8).
Use in Elderly Patients: Monitor for signs and symptoms of osteoarthritis (1.1, 2).

ADVERSE REACTIONS

- Most common (≥5%) and general side effects: abdominal pain, headache, dizziness, upper respiratory tract infections, dyspepsia, and influenza-like symptoms (4.1)
- Adverse events observed in pediatric studies were similar to those in adults who received oral meloxicam (4.2)

To report SUSPECTED ADVERSE REACTIONS, contact Opiurna Pharmaceuticals (USA), Inc. at 1-866-362-4916 or PRA at 1-866-THE-1111 or www.opiurna.com.

DRUG INTERACTIONS

- **Drug-Drug Interactions with NSAIDs:** Do not use Meloxicam Tablets USP with aspirin, ibuprofen, or other NSAIDs (5.1).
Drug-Drug Interactions with PPIs: Do not use Meloxicam Tablets USP with PPIs (5.1).
Drug-Drug Interactions with Aspirin: Do not use Meloxicam Tablets USP with aspirin (5.1).
Drug-Drug Interactions with ACE Inhibitors: Do not use Meloxicam Tablets USP with ACE inhibitors (5.1).
Drug-Drug Interactions with Diuretics: Do not use Meloxicam Tablets USP with diuretics (5.1).
Drug-Drug Interactions with Anticoagulants: Do not use Meloxicam Tablets USP with anticoagulants (5.1).
Drug-Drug Interactions with Antagonists: Do not use Meloxicam Tablets USP with antagonists (5.1).
Drug-Drug Interactions with Anticholinergics: Do not use Meloxicam Tablets USP with anticholinergics (5.1).
Drug-Drug Interactions with Insulin: Do not use Meloxicam Tablets USP with insulin (5.1).
Drug-Drug Interactions with Oral Hypoglycemics: Do not use Meloxicam Tablets USP with oral hypoglycemics (5.1).
Drug-Drug Interactions with Antidepressants: Do not use Meloxicam Tablets USP with antidepressants (5.1).
Drug-Drug Interactions with Antipsychotics: Do not use Meloxicam Tablets USP with antipsychotics (5.1).
Drug-Drug Interactions with Antiepileptics: Do not use Meloxicam Tablets USP with antiepileptics (5.1).
Drug-Drug Interactions with Antifungals: Do not use Meloxicam Tablets USP with antifungals (5.1).
Drug-Drug Interactions with Antivirals: Do not use Meloxicam Tablets USP with antivirals (5.1).
Drug-Drug Interactions with Immunosuppressants: Do not use Meloxicam Tablets USP with immunosuppressants (5.1).
Drug-Drug Interactions with Hormonal Contraceptives: Do not use Meloxicam Tablets USP with hormonal contraceptives (5.1).

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Use with caution during the first trimester of pregnancy because of the potential for miscarriage and/or fetal death. Avoid use of NSAIDs in pregnant women starting at 30 weeks gestation (5.4, B.1).
- **Lactation:** NSAIDs are excreted with reversible ability. Consider withdrawal of Meloxicam in women who have difficulty conceiving (4.3).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 1/2018

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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)).
- Meloxicam tablets are contraindicated in the setting of coronary artery bypass graft (CABG) surgery (see Contraindications (4) and 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 upper GI bleeding are at greater risk for serious GI events (see Warnings and Precautions (5.2)).

1 INDICATIONS AND USAGE

1.1 Osteoarthritis (OA)
Meloxicam tablets are indicated for relief of the signs and symptoms of osteoarthritis (see Clinical Studies (14.1)).

1.2 Rheumatoid Arthritis (RA)
Meloxicam tablets are indicated for relief of the signs and symptoms of rheumatoid arthritis (see Clinical Studies (14.1)).

1.3 Juvenile Rheumatoid Arthritis (JRA) Pauciarticular and Polyarticular Course
Meloxicam tablets are indicated for relief of the signs and symptoms of pauciarticular or polyarticular course juvenile Rheumatoid Arthritis in patients who weigh ≥60 kg (see Dosage and Administration (2.4) and Clinical Studies (14.2)).

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Instructions
Carefully consider the potential benefits and risks of Meloxicam tablets and other treatment options before deciding to use Meloxicam tablets. Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals (see Warnings and Precautions (3)).

After observing the response to initial therapy with Meloxicam tablets, adjust the dose to suit an individual patient's needs.
In adults, the maximum recommended daily oral dose of Meloxicam tablets is 15 mg regardless of formulation. In patients with renal dysfunction, a maximum daily dosage of 7.5 mg is recommended (see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)).
Meloxicam tablets may be taken without regard to timing of meals.

2.2 Osteoarthritis
For the relief of the signs and symptoms of osteoarthritis the recommended starting and maintenance oral dose of Meloxicam tablets is 7.5 mg once daily. Some patients may receive additional benefit by increasing the dose to 15 mg once daily.

2.3 Rheumatoid Arthritis
For the relief of the signs and symptoms of rheumatoid arthritis, the recommended starting and maintenance oral dose of Meloxicam tablets is 15 mg once daily. Some patients may receive additional benefit by increasing the dose to 15 mg once daily.

2.4 Juvenile Rheumatoid Arthritis (JRA) Pauciarticular and Polyarticular Course
For the treatment of juvenile rheumatoid arthritis, the recommended dose of Meloxicam tablets is 7.5 mg once daily in children who weigh ≥60 kg. There is no additional benefit demonstrated by increasing the dose above 7.5 mg in clinical trials.
Meloxicam tablets should not be used in children who weigh <60 kg.

2.5 Renal Impairment
The use of Meloxicam tablets in subjects with severe renal impairment is not recommended. In patients with renal dysfunction, the maximum dosage of Meloxicam tablets is 7.5 mg per day (see Clinical Pharmacology (12.3)).

2.6 Non-Interchangeability with Other Formulations of Meloxicam
Meloxicam tablets have not been shown equivalent systemic exposure to other approved formulations of oral meloxicam. Therefore, Meloxicam tablets are not interchangeable with other formulations of oral meloxicam.

meiotic product even if the total milligram strength is the same. Do not substitute similar dose strengths of Meloxicam tablets with other formulations of oral meloxicam product.

3 DOSAGE FORMS AND STRENGTHS

Meloxicam Tablets USP:

- 7.5 mg: Light yellow, round flat beveled edged, tablet with U & L debossed on one side and 7.5 debossed centrally on the other side
- 15 mg: Light yellow, capsule shaped, biconvex, tablet with U & L debossed on one side and 15 debossed centrally on the other side

4 CONTRAINDICATIONS

Meloxicam tablets are contraindicated in the following patients:

- Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to meloxicam or any components of the drug product [see Warnings and Precautions (5.7, 5.9)]
- 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)]
- 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 week 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 meloxicam, increases the risk of serious gastrointestinal (GI) events [see Warnings and Precautions (5.2)].

5.2 Serious 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 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke. NSAIDs are contraindicated in the setting of CABG [see Contraindications (4)].

5.3 Real Toxicity

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. Initial case cohorts, 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 first four years of follow-up.

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

5.4 Gastrointestinal Bleeding, Ulceration, and Perforation

NSAIDs, including meloxicam, can 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 events observed with celecoxib can be fatal and in some cases without warning symptoms. Ulcerations treated with NSAIDs. Only one in five patients who develop a serious upper GI adverse event on NSAID therapy is symptomatic. Upper GI adverse events, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3-6 months, and in about 2-4% of patients treated for one year. However, even short-term NSAID therapy is not without risk.

5.5 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 may increase the risk of GI bleeding in patients treated with NSAIDs include longer duration of NSAID therapy; concomitant use of anticoagulants, aspirin, antiplatelets, or selective serotonin reuptake inhibitors (SSRIs); history of alcoholism, age, and prior peptic ulcer disease. 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.

5.6 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 Meloxicam until a serious GI adverse event is ruled out.
- In the setting of concurrent use of low-dose aspirin for cardiac prophylaxis, monitor patients more closely for evidence of GI bleeding [see Drug Interactions (7)].

5.7 Hepatotoxicity

Elevation 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.

Elevation of ALT or AST (less than three times ULN) may occur in up to 15% of patients treated with NSAIDs, including meloxicam. Symptoms of the warning signs and symptoms of hepatotoxicity (e.g., anorexia, fatigue, lethargy, darkening of urine, 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 Meloxicam immediately and perform a clinical evaluation of the patient [see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)].

5.8 Hypertension

NSAIDs, including Meloxicam, can lead to new onset 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, thiazide diuretics, or loop diuretics may have impaired response to these therapies when taking NSAIDs [see Drug Interactions (7)]. Monitor blood pressure (BP) during the initiation of NSAID treatment and throughout the course of therapy.

5.9 Heart Failure and Edema

The Cox-2 and traditional NSAID Trialists' Collaboration meta-analysis of randomized controlled trials demonstrated an approximately two-fold increase in hospitalization 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 meloxicam 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)].

Avoid the use of Meloxicam in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If Meloxicam is used in patients with severe heart failure, monitor patients for signs of worsening heart failure.

5.6 Renal Toxicity and Hypokalemia

Renal Toxicity

Long-term administration of NSAIDs, including Meloxicam, has resulted in renal papillary necrosis, renal insufficiency, acute renal failure, and other renal injury.

Renal toxicity has also been reported 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 renal prostaglandin formation, and, consequently, an increase in renal blood flow, which may precipitate acute 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 in the pre-renal state.

The renal effects of Meloxicam may hasten the progression of renal dysfunction in patients with pre-existing renal disease. Because some Meloxicam metabolites are excreted by the kidney, monitor patients for signs of worsening renal function.

Correct volume status in dehydrated or hypovolemic patients prior to initiating Meloxicam. Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia during use of Meloxicam [see Drug Interactions (7)].

No information is available from controlled clinical studies regarding the use of Meloxicam in patients with advanced renal disease. Avoid the use of Meloxicam in patients with advanced renal disease unless the benefits are expected to outweigh the risk of worsening renal function. If Meloxicam is used in patients with advanced renal disease, monitor patients for signs of worsening renal function [see Clinical Pharmacology (12.3)].

Hypokalemia

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, hypoadrenergic state.

5.7 Anaphylactic Reactions

Meloxicam has been associated with anaphylactic reactions in patients with and without known hypersensitivity to meloxicam and in patients with aspirin-sensitive asthma [see Contraindications (4) and Warnings and Precautions (5.8)].

Seek emergency help if an anaphylactic reaction occurs.

5.8 Cross-Reactions 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, Meloxicam is contraindicated in patients with this form of asthma sensitivity [see Contraindications (4)]. When Meloxicam 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 meloxicam, can cause serious skin adverse reactions such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Inform patients about the signs and symptoms of serious skin reactions, and to discontinue the use of Meloxicam at the first appearance of skin rash or any other sign of hypersensitivity. Meloxicam is contraindicated in patients with previous serious skin reactions to NSAIDs [see Contraindications (4)].

5.10 Premature Closure of Fetal Ductus Arteriosus

Meloxicam may cause premature closure of the fetal ductus arteriosus. Avoid use of NSAIDs, including Meloxicam, in pregnant women starting at 30 weeks of gestation (third trimester) [see Use in Specific Populations (8.1)].

5.11 Hematologic Toxicity

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

NSAIDs, including Meloxicam, may increase the risk of bleeding events. Co-morbid conditions such as coagulation disorders or concomitant use of warfarin, other anti-coagulants, 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)].

5.12 Masking of Inflammation and Fever

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

5.13 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 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 Risk Factor Warnings and Precautions (5.1)]
- GI Bleeding, Ulceration, and Perforation [see Risk Factor 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 Hypokalemia [see Warnings and Precautions (5.6)]
- Anaphylactic Reactions [see Warnings and Precautions (5.7)]
- Serious Skin Reactions [see Warnings and Precautions (5.9)]
- Hematologic Toxicity [see Warnings and Precautions (5.11)]

6.1 Clinical Trial Experience

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

6.2 Discontinuation and Hemorrhagic Anemia

The Meloxicam Phase 2-3 clinical trial database includes 10,122 OA patients and 1012 RA patients treated with Meloxicam 7.5 mg/day, 1505 OA patients and 1351 RA patients treated with Meloxicam 15 mg/day. Meloxicam in these doses was administered to 661 patients for at least 6 months and to 312

Clinical Considerations

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

Dose

Animal Data

Meloxicam was not teratogenic when administered to pregnant rats during fetal organogenesis at oral doses up to 4 mg/kg/day (2.5-fold greater than the MTD of 1.5 mg/kg of Meloxicam based on BSA comparison). Administration of meloxicam to pregnant rabbits throughout embryogenesis produced an increased incidence of septal defects of the heart at an oral dose of 50 mg/kg/day (35-fold greater than the MTD based on BSA comparison). The no effect level was 20 mg/kg/day (13-fold greater than the MTD based on BSA comparison). In rats and rabbits, embryofetality occurred at oral meloxicam doses of 1 mg/kg/day and 2 mg/kg/day, respectively (0.65-fold greater, respectively, than the MTD based on BSA comparison) when administered throughout organogenesis.

Oral administration of meloxicam to pregnant rats during late gestation through lactation increased the incidence of dystocia, delayed parturition, and decreased offspring survival at meloxicam doses of 0.125 mg/kg/day or greater (0.083-fold greater MTD based on BSA comparison).

8.2 Lactation

Risk Summary

There are no human data available on whether meloxicam is present in human milk, or on the effects on breastfed infants, or on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Meloxicam and any potential adverse effects on the breastfed infant from the Meloxicam from the underlying maternal condition.

Dose

Animal Data

Meloxicam was present in the milk of lactating rats at concentrations higher than those in plasma.

8.3 Females and Males of Reproductive Potential

Infertility

Females

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

8.4 Pediatric Use

The safety and effectiveness of meloxicam in pediatric JRA patients from 2 to 17 years of age has been evaluated in three clinical trials (see *Dosage and Administration (2.3), Adverse Reactions (6.1) and Clinical Studies (14.2)*).

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, 5.10)*).

8.6 Hepatic Impairment

No dose adjustment is necessary in patients with mild to moderate hepatic impairment. Patients with severe hepatic impairment have not been adequately studied. Since meloxicam is not significantly metabolized in the liver and hepatotoxicity may occur, use meloxicam with caution in patients with hepatic impairment (see *Warnings and Precautions (5.3) and Clinical Pharmacology (12.3)*).

8.7 Renal Impairment

No dose adjustment is necessary in patients with mild to moderate renal impairment. Patients with severe renal impairment have not been studied. The use of Meloxicam in subjects with severe renal impairment is not recommended. In patients on hemodialysis, meloxicam should not exceed 7.5 mg per day. Meloxicam is not dialyzable (see *Dosage and Administration (2.1) and Clinical Pharmacology (12.3)*).

10 OVERDOSAGE

Symptoms following acute NSAID overdosage 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)*).

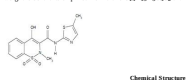
Manage patients with symptomatic and supportive care following an NSAID overdosage. There are no specific antidotes. Consider emesis and/or activated charcoal (50 to 100 grams in adults, 1 to 2 grams per kg of body weight in pediatric patients) and/or osmotic cathartic in symptomatic patients seen within four hours of ingestion in patients with a large overdosage (5 to 10 times the recommended dosage). Forced diuresis, alkalization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

There is limited experience with meloxicam overdosage. Cholestyramine is known to accelerate the clearance of meloxicam. Accelerated removal of meloxicam by 4 g oral doses of cholestyramine given three times a day was demonstrated in a clinical trial. Administration of cholestyramine may be useful following an overdosage.

For additional information about overdosage treatment, call a poison control center (1-800-322-2222).

11 DESCRIPTION

Meloxicam Tablets USP are a nonsteroidal anti-inflammatory drug (NSAID). Each tablet contains 7.5 mg or 15 mg meloxicam for oral administration. Meloxicam is chemically designated as 4-hydroxy-2-methyl-5-(2-methyl-5-thiazolidyl)-2H-1,2,4-thiazolidin-3-carboxamide, 1,1-dioxide. The molecular weight is 351.4. Its empirical formula is $C_{14}H_{17}N_3O_5S_2$ and it has the following structural formula:



Meloxicam is a pale yellow solid, practically insoluble in water, with higher solubility observed in strong acids and bases. It is very slightly soluble in methanol. Meloxicam has an apparent partition coefficient (log *P*) of 1.1 in octanol:buffer (pH 7.4). Meloxicam has *p*K_a values of 1.1 and 4.2. Meloxicam is available as a tablet for oral administration containing 7.5 mg or 15 mg meloxicam.

The inactive ingredients in Meloxicam tablets USP include colloidal silicon dioxide, croscarmellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyvinylpyrrolidone, and hydroxypropylcellulose.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Meloxicam has analgesic, anti-inflammatory, and antipyretic properties. The mechanism of action of Meloxicam, like that of other NSAIDs, is not completely understood but involves inhibition of cyclooxygenase (COX-1 and COX-2).

Meloxicam is a potent inhibitor of prostaglandin synthesis in vivo. Meloxicam concentrations reached during therapy have produced no *in vivo* effects. Prostaglandins, which affect renal and potassium channels of the kidney, are important in maintaining renal function. Prostaglandins are mediators of inflammation because meloxicam is an inhibitor of prostaglandin synthesis, its mode of action may be due to a decrease of prostaglandin in peripheral tissues.

12.2 Pharmacokinetics

Absorption

The absolute bioavailability of meloxicam capsules was 89% following a single oral dose of 30 mg compared with 30 mg IV bolus injection. Following single intravenous doses, dose-proportional pharmacokinetics were shown in the range of 5 mg to 60 mg. After multiple oral doses, the pharmacokinetics of meloxicam capsules were dose-proportional over the range of 7.5 mg to 15 mg. Mean C_{max} was achieved within four to five hours after a 7.5 mg meloxicam tablet was taken under fasted conditions, indicating a prolonged drug absorption. With multiple dosing, steady-state concentrations were reached by Day 5. A second meloxicam concentration peak occurs around 12 to 14 hours post-dose suggesting biliary recycling.

Meloxicam capsules have been shown to be bioequivalent to Meloxicam tablets.

Table 4 Single Dose and Steady-State Pharmacokinetic Parameters for Oral 7.5 mg and 15 mg Meloxicam (Mean and % CV)^a

Pharmacokinetic Parameters (%CV)	Steady State		Single Dose	
	7.5 mg capsules	15 mg capsules	7.5 mg capsules	15 mg capsules
N	10	5	8	12
C _{max} (ng/mL)	1.02 (20)	2.1 (20)	3.2 (24)	6.79 (26)
t _{max} (h)	4.9 (10)	1.1 (2)	6.1 (27)	4.0 (25)
C _{12h} (ng/mL)	20 (14)	34 (14)	26 (14)	45 (20)
C _{12h} (ng/mL)	8.8 (20)	9.9 (20)	10 (43)	11 (44)
AUC _{0-12h} (ng·h/mL)	14.7 (12)	15 (42)	10 (30)	20 (44)

^a The parameter values in the table are from various studies.

^b *n* = under high fat conditions.

^c Meloxicam tablets.

^d *n* = 1 (AUC=NA)

Food and Amount of Effect

Administration of meloxicam capsules following a high fat breakfast (75% of fat) resulted in mean peak drug levels (i.e., C_{max}) being increased by approximately 22%, while the extent of absorption (AUC) was unchanged. The time to maximum concentration (t_{max}) was also decreased from 5 to 4 hours. No pharmacokinetic interaction was detected with concomitant administration of antacid. Based on these results, Meloxicam can be administered without regard to timing of meals or concomitant administration of antacid.

Distribution

The mean volume of distribution (V_d) of meloxicam is approximately 10 L. Meloxicam is ~99.4% bound to human plasma protein (primarily albumin) within the therapeutic dose range. The fraction of protein binding, independent of drug concentration, over the clinically relevant concentration range, but decreases to ~95% in patients with renal disease. Meloxicam penetration into human blood cells, after oral dosing, is less than 10%. Following a radiolabeled dose, over 90% of the radioactivity dose in the plasma was present as unchanged meloxicam.

Meloxicam concentrations in synovial fluid, after a single oral dose, range from 40% to 50% of those in plasma. The free fraction in synovial fluid is 2.5 times higher than in plasma, due to the lower albumin content in synovial fluid as compared to plasma. The significance of this penetration is unknown.

Metabolism

Meloxicam is extensively metabolized in the liver. Meloxicam metabolites include 5-carboxy meloxicam (60% of dose), from 4-*o*-hydroxy meloxicam formed by oxidation of an immediate metabolite 5-hydroxymethyl meloxicam which is also excreted to a lesser extent (9% of dose). *In vivo* studies indicate that CYP2C9 cytochrome P450 metabolizing enzyme plays an important role in the metabolic pathway with a minor contribution of the CYP3A4 isozyme. Patient's peroxidase activity is probably responsible for the other two metabolites which account for 30% and 4% of the administered dose, respectively. All the four metabolites are not known to have any *in vivo* pharmacological activity.

Excretion

Meloxicam excreted predominantly in the form of metabolites, and occurs to equal extent in the urine and feces. Only traces of the unchanged parent compound were excreted in the urine (2% and 1.8%) and feces (1.8%). The extent of the urinary excretion was confirmed for radiolabeled multiple 7.5 mg doses: 0.5%, 6%, and 13% of the dose were found in urine in the form of meloxicam, and the 5-hydroxymethyl and 5-carboxy metabolites, respectively. There is significant biliary and/or renal excretion of the drug. This was demonstrated when oral administration of cholestyramine following a single IV dose of meloxicam decreased the AUC of meloxicam by 50%.

The mean elimination half-life (t_{1/2}) ranges from 15 hours to 20 hours. The elimination half-life is constant across dose levels indicating linear metabolism within the therapeutic dose range. Plasma clearance ranges from 7 to 9 mL/min.

Specific Population

Pediatric

A single (0.25 mg/kg) dose administration and after achieving steady state (0.375 mg/kg/day) there was a general trend of approximately 30% lower exposure in younger patients (2 to 6 years old) as compared to the older patients (7 to 16 years old). The other patients had meloxicam exposure similar (single doses) or slightly reduced (steady state) to those in the adult patients, when using AUC values normalized to a dose of 15 mg/kg/day (see *Dosage and Administration (2.4)*). The meloxicam mean (SD) elimination half-life was 15.2 (10.1) and 13.0 hours (10) for the 2 to 6 year old patients, and 7 to 16 year old patients, respectively.

In a covariate analysis, utilizing population pharmacokinetics, body-weight, but not age, was the single predictive covariate for differences in the meloxicam apparent plasma clearance. The body-weight normalized apparent oral clearance values were adequate predictors of meloxicam exposure in pediatric patients.

The pharmacokinetics of Meloxicam in pediatric patients under 2 years of age have not been investigated.

Geriatric

Elderly males (65 years of age) exhibited meloxicam plasma concentrations and steady-state pharmacokinetics similar to young males. Elderly females (65 years of age) had a 47% higher AUC and 12% higher C_{max} as compared to younger females (55 years of age) after both body weight normalization. Despite the increased oral concentrations in the elderly females, the adverse event profile was comparable for both elderly patient populations. A similar free fraction was found in elderly female patients in comparison to elderly male patients.

Sex

Young females exhibited slightly lower plasma concentrations relative to young males. After single doses of 7.5 mg Meloxicam, the mean elimination half-life was 19.5 hours for the female group as compared to 23.2 hours for the male group. At steady state, the data were similar (17.5 hours vs. 21.4 hours). This pharmacokinetic difference due to gender is likely to be of little clinical importance. There was linearity of pharmacokinetics and no appreciable differences in the C_{max} or T_{max} across genders.

Hepatic Impairment

Following a single 15 mg dose of meloxicam there was no marked difference in plasma concentrations in patients with mild (Child-Pugh Class I) to moderate (Child-Pugh Class II) hepatic impairment compared to healthy volunteers. Protein binding of meloxicam was not affected by hepatic impairment. No dosage adjustment is necessary in patients with mild to moderate hepatic impairment. Patients with severe hepatic impairment (Child-Pugh Class III) have not been adequately studied (see *Warnings and Precautions (5.3) and Use in Specific Populations (6.6)*).

Renal Impairment

Meloxicam pharmacokinetics have been investigated in subjects with mild and moderate renal impairment. Total drug plasma concentration of meloxicam decreased and half-life/clearance of meloxicam increased with the degree of renal impairment while free AUC values were similar in all groups. The higher meloxicam clearance in subjects with renal impairment may be due to increased fractional tubular secretion of meloxicam which is available for hepatic metabolism and subsequent excretion. No dosage adjustment is necessary in patients with mild to moderate renal impairment. Patients with severe renal impairment have not been adequately studied. The use of Meloxicam in subjects with severe renal impairment is not recommended (see Dosage and Administration (2.3), Warnings and Precautions (5.5) and Use in Specific Populations (8.7)).

Hemostatics

Following a single dose of meloxicam, the free Cmax plasma concentration were higher in patients with renal failure on chronic hemodialysis (1% free fraction) in comparison to healthy volunteers (0.2% free fraction). Hemodialysis did not lower the total drug concentration in plasma; therefore, additional doses are not necessary after hemodialysis. Meloxicam is not dialyzable (see Dosage and Administration (2.1) and Use in Specific Populations (8.7)).

Drug Interactions Studies

Aspirin: When NSAIDs were administered with aspirin, the plasma half-life of NSAIDs were reduced, although the clearance of free NSAID was not altered. When Meloxicam was administered with aspirin (100 mg three times daily) to healthy volunteers, it tended to increase the AUC₀₋₂₄ (10% and Cmax (24%) of meloxicam. The clinical significance of this interaction is not known. See Table 3 for clinically significant drug interactions of NSAIDs with aspirin (see Drug Interactions (7)).

Cholestyramine: Pretreatment for four days with cholestyramine significantly increased the clearance of meloxicam by 50%. This resulted in a decrease in t_{1/2} from 19.2 hours to 12.5 hours, and a 30% reduction in AUC. This suggests the existence of a recirculation pathway for meloxicam in the gastrointestinal tract. The clinical relevance of this interaction has not been established.

Clopidogrel: Concurrent administration of 300 mg clopidogrel four times daily did not alter the single-dose pharmacokinetics of 30 mg meloxicam.

Digoxin: Meloxicam 15 mg once daily for 7 days did not alter the plasma concentration profile of digoxin after 5-epivigilant administration for 7 days at clinical doses. In vitro testing found no protein binding drug interaction between digoxin and meloxicam.

Lithium: In a study conducted in healthy subjects, mean pre-dose lithium concentration and AUC were increased by 21% in subjects receiving lithium doses ranging from 804 to 1072 mg twice daily with meloxicam 15 mg QD every day as compared to subjects receiving lithium alone (see Drug Interactions (7)).

Methotrexate: A study in 13 rheumatoid arthritis (RA) patients evaluated the effects of multiple doses of meloxicam on the pharmacokinetics of methotrexate tolerance weekly. Meloxicam did not have significant effect on the pharmacokinetics of single doses of methotrexate. In vitro, methotrexate did not displace meloxicam from its human serum binding sites (see Drug Interactions (7)).

Warfarin: The effect of meloxicam on the anticoagulant effect of warfarin was studied in a group of healthy subjects receiving daily doses of warfarin (produced an INR (International Normalized Ratio) between 1.2 and 1.8). In these subjects, meloxicam did not alter warfarin pharmacokinetics and the average anticoagulant effect of warfarin as determined by prothrombin time. However, one subject showed an increase in INR from 1.5 to 2.1. Caution should be used when administering Meloxicam with warfarin patients on warfarin therapy. Changes in INR and an increased risk of bleeding complications when a new medication is introduced (see Drug Interactions (7)).

11 NONCLINICAL TOXICOLOGY

11.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

There was no increase in tumor incidence in long-term carcinogenicity studies in rats (104 weeks) and mice (97 weeks) administered meloxicam oral doses up to 8 mg/kg/day in rats and up to 8.0 mg/kg/day in mice (up to 0- and 2.6-times, respectively, the maximum recommended human dose (MRHD) of 15 mg/day Meloxicam based on body surface area (BSA) comparison).

Mutagenesis

Meloxicam was not mutagenic in an Ames assay, or clastogenic in a chromosome aberration assay with human lymphocytes and in *in vivo* micronucleus test in mouse bone marrow.

Impairment of Fertility

Meloxicam did not impact male and female fertility in rats at oral doses up to 8 mg/kg/day in males and 5 mg/kg/day in females (up to 5.8- and 3.2-times greater, respectively, than the MRHD based on BSA comparison).

14 CLINICAL STUDIES

14.1 Osteoarthritis and Rheumatoid Arthritis

The use of Meloxicam for the treatment of the signs and symptoms of osteoarthritis of the knee and hip was evaluated in a 12-week, double-blind, controlled trial. Meloxicam (7.5 mg, 7.5 mg, and 15 mg daily) was compared to placebo. The four primary endpoints were investigator global assessment, patient global assessment, patient pain assessment, and total WOMAC score (a self-administered questionnaire addressing pain, function, and stiffness). Patients on Meloxicam 7.5 mg daily and Meloxicam 15 mg daily showed significant improvement in each of these endpoints compared with placebo.

The use of Meloxicam for the management of signs and symptoms of rheumatoid arthritis was evaluated in a 12-week, double-blind, active-controlled trial outside the U.S. ranging from 4 weeks to 6 months duration. In these trials, the efficacy of Meloxicam, in doses of 7.5 mg daily and 15 mg/day, was comparable to piroxicam 20 mg/day and diclofenac SR 100 mg/day and consistent with the efficacy seen in the U.S. trial.

The use of Meloxicam for the treatment of the signs and symptoms of rheumatoid arthritis was evaluated in a 12-week, double-blind, controlled multicenter trial. Meloxicam (7.5 mg, 15 mg, and 22.5 mg daily) was compared to placebo. The primary endpoint in this study was the ACR20 response rate, a composite measure of clinical, laboratory, and functional measures of RA response. Patients receiving Meloxicam 7.5 mg and 15 mg daily showed significant improvement in the primary endpoint compared with placebo. No incremental benefit was observed with the 22.5 mg dose compared to the 15 mg dose.

14.2 Juvenile Rheumatoid Arthritis (JRA) Pauciarticular and Polyarticular Course

The use of Meloxicam for the treatment of the signs and symptoms of pauciarticular or polyarticular course Juvenile Rheumatoid Arthritis in patients 2 years of age and older was evaluated in two 12-week, double-blind, parallel-arm, active-controlled trials.

Both studies included three arms: naproxen and two doses of meloxicam. In both studies, meloxicam dosing began at 0.25 mg/kg/day (7.5 mg maximum) or 0.25 mg/kg/day (15 mg maximum) and naproxen dosing began at 10 mg/kg/day. One study used these doses throughout the 12-week dosing period, while the other incorporated a reduction after 4 weeks to doses of 0.25 mg/kg/day and 0.375 mg/kg/day (2.5 mg maximum) of meloxicam and 15 mg/kg/day of naproxen.

The efficacy analysis used the ACR Pediatric 20 responder definition, a composite of parent and investigator assessments, counts of active joints, and joint with limited range of motion, and erythrocyte sedimentation rate. The proportion of responders were similar in all three groups in both studies, and no difference was observed between the meloxicam dose groups.

16 HOW SUPPLIED/STORAGE AND HANDLING

Meloxicam tablets USP are available as a light yellow, round, flat, uncoated tablet containing meloxicam 7.5 mg or a light yellow, oblong, beveled, uncoated tablet containing meloxicam 15 mg. The 7.5 mg tablet is impressed with linear 1 and 1, on one side and tablet code 7.5 on the other side. The 15 mg tablet is impressed with linear 1 and 1, on one side and tablet code 15 on the other side.

Meloxicam Tablets USP 7.5 mg are available as follows:

NDC 29300-124-13, Bottles of 30

NDC 29300-124-01, Bottles of 100

NDC 29300-124-10, Bottles of 1000

NDC 29300-124-50, Bottles of 5000

Meloxicam Tablets USP 15 mg are available as follows:

NDC 29300-125-13, Bottles of 30

NDC 29300-125-01, Bottles of 100

NDC 29300-125-10, Bottles of 1000

NDC 29300-125-50, Bottles of 5000

Storage: Store at 20° to 25° (68° to 77°F) [see USP Controlled Room Temperature]. Keep Meloxicam Tablets USP in a dry place.

Dispense tablets in a tight container.

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

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide) that accompanies each prescription dispensed.

Additional Medication Guides can be obtained by calling Unichem at 1-866-562-4616.

Inform patients, families or their caregivers of the following information before initiating therapy with an NSAID 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 health care 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, reflux, and hematemesis in their health care provider. In the setting of concurrent use of low-dose aspirin for cardiac prophylaxis, inform patients of the increased risk for the signs and symptoms of GI bleeding (see Warnings and Precautions (5.2)).

Hypotension

Inform patients of the warning signs and symptoms of hypotension (e.g., nausea, fatigue, lethargy, dizziness, syncope, jaundice, light upper extremity tenderness, and "the flu") symptoms. If these occur, instruct patients to stop Meloxicam tablets 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 health care 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) and Warnings and Precautions (5.7)).

Serious Skin Reactions

Advise patients to stop Meloxicam tablets immediately if they develop any type of rash and to contact their health care provider as soon as possible (see Warnings and Precautions (5.6)).

Female Fertility

Advise females of reproductive potential who desire pregnancy that NSAIDs, including Meloxicam tablets, may be associated with a reversible delay in ovulation (see Use in Specific Populations (8.1)).

Fetal Toxicity

Inform pregnant women to avoid use of Meloxicam tablets and other NSAIDs starting at 30 weeks gestation because of the risk of the premature closing of the fetal ductus arteriosus (see Warnings and Precautions (5.10) and Use in Specific Populations (8.1)).

Avoid Concurrent Use of NSAIDs

Inform patients that the concurrent use of Meloxicam tablets with other NSAIDs or salicylates (e.g., difflural, salicylate) is not recommended due to the increased risk of gastrointestinal toxicity, and little or no increase in efficacy (see Warnings and Precautions (5.2) and Drug Interactions (7)). Advise patients that NSAIDs may be present in "over the counter" medications for treatment of colds, fever, or aches.

Use of NSAIDs and Low-Dose Aspirin

Inform patients not to use low-dose aspirin concurrently with Meloxicam tablets until they talk to their health care provider (see Drug Interactions (7)).

For current prescribing information, call Unichem at 1-866-562-4616.

Manufactured by:

UNICHEM LABORATORIES LTD.

Pilore Ind. Estate,

Pilore, Raipur, G.S. 403111, India

Marketed by:



Unichem Logo

Hatfield Heights, NJ 07604

06-8-09/2016

1308865

Medication Guide for Non-steroidal Anti-inflammatory Drugs (NSAIDs)

What is the most important information I should know about medicines called Non-steroidal 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.
- with increasing doses of NSAIDs
- with longer use of NSAIDs

Do not take NSAIDs right before or after a heart surgery called a "coronary artery bypass graft (CABG)."

Avoid taking NSAIDs after a recent heart attack, unless your health care 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 (perforations) 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 (ulcer medicines called "proton-pump inhibitors," "anticoagulants," "SSRIs," or "SNRIs")

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

NSAIDs should only be used:

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

What are NSAIDs?

NSAIDs are used to treat pain and reduce, 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. Talk to your healthcare provider if you are considering taking NSAIDs during pregnancy. You should not take NSAIDs after 29 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 hives with fever
- swelling of the arm, legs, hand and feet

If you take too much of your NSAID, call your healthcare provider or get medical help right away. These are not 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 it was not prescribed. Do not give NSAIDs to other people, even if they have the same symptoms that you have. It may harm them.

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

Additional Medication Guides can be obtained by calling Unichem at 1-866-562-4616.

The other trademarks referenced are owned by third parties not affiliated with Unichem Laboratories Limited.

Manufactured by:
UNICHEM LABORATORIES LTD.

Pôrtovo Ind. Estate,
Pôrtovo, Goa 403511, India

Marketed by:



Unichem Logo

Haberstock Heights, NJ 07064

05-8-09-2016

1308865

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

Revised: September 2016

PACKAGE LABEL-PRINCIPAL DISPLAY PANEL

Sample - Not for sale
Dissolve: See package insert

Store at Controlled
Room Temperature

UNICHEM LABORATORIES LTD.
Pôrtovo Ind. Estate,
Pôrtovo, Goa 403511, India

Meloxicam Tablets
USP, 7.5mg
30 Tablets

Take _____ (tab)(s)
_____ time(s) daily or
every _____ hour(s)
for _____ day(s).

See the Other(s) In
Case Pack, N13762

Keep container tightly closed
Keep out of reach of children

Rx Only

Meloxicam Tablets USP 7.5 mg

MELOXICAM			
meloxicam tablet			
Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	NDA Code (Number)	NDC 42708-018-30 (NDC-18 301-018)
Route of Administration	ORAL		
Active Ingredient/Active Moiety			
	Ingredient Name	Route of Strength	Strength
MELOXICAM (018 VEGICAPICAM) (UNICHEM LABORATORIES LTD.)	MELOXICAM		7.5 mg
Inactive Ingredients			
	Ingredient Name		Strength
MELOXICAM (UNICHEM LABORATORIES LTD.)	CELLULOSE (UNICHEM LABORATORIES LTD.)		
MELOXICAM (UNICHEM LABORATORIES LTD.)	DIHYDROGEN PHOSPHATE (UNICHEM LABORATORIES LTD.)		
MELOXICAM (UNICHEM LABORATORIES LTD.)	LACTOSE MONOHYDRATE (UNICHEM LABORATORIES LTD.)		
MELOXICAM (UNICHEM LABORATORIES LTD.)	METHACRYLIC ACID (UNICHEM LABORATORIES LTD.)		
MELOXICAM (UNICHEM LABORATORIES LTD.)	POLYBUTYLENE TEREPHTHALATE (UNICHEM LABORATORIES LTD.)		
MELOXICAM (UNICHEM LABORATORIES LTD.)	STEARIC ACID (UNICHEM LABORATORIES LTD.)		
MELOXICAM (UNICHEM LABORATORIES LTD.)	TITANIUM DIOXIDE (UNICHEM LABORATORIES LTD.)		
Product Characteristics			
Color	YELLOW	Shape	ROUNDED
Shape	ROUNDED	Size	7mm
Imprint	UNICHEM	Imprint Code	UNICHEM
Container			
Packaging			
1 - NDC Code	Package Description	Marketing Start Date	Marketing End Date
1 - NDC 42708-018-30 (30 in 1) (MOTILE) Type 0: Not a Combination Product	30 (30) (30)	11/12/2016	
Marketing Information			
Marketing Category	Application Number and Marketing Classification	Marketing Status Date	Marketing End Date
ANDA	ANDA 071927	03/15/2017	
Labels - QPharma Inc. (03020888)			
Registrant - Unichem Pharmaceuticals (USA), Inc. (01802016)			
Establishment			
Name	Address	BSN1	Business Operations
Unichem Pharmaceuticals	18010104	(018) (018) (018)	(018) (018) (018)

Revised: 01/2019

QPharma Inc.