Meloxicam Tablets, USP:

3 DOSAGE FORMS AND STRENGTHS

Meloxicam tablets have not shown equivalent systemic exposure to other approved formulations of oral Meloxicam product even if the total milligram strength is the same. Do not substitute similar dose strengths.

7.5 mg once daily in children who weigh ≥60 kg. There was no additional benefit demonstrated by increasing the dose above 7.5 mg once daily.

In patients on hemodialysis, the maximum dosage of meloxicam is 7.5 mg per day and should be administered as a single dose in the morning at least 12 hours after the dialysis session.

In patients with impaired renal function, the starting dose of either meloxicam tablets, meloxicam capsules, or meloxicam elixir should be 7.5 mg once daily. In patients with severe renal impairment, including patients on hemodialysis, the maximum dosage of meloxicam is 7.5 mg per day.

Carefully consider the potential benefits and risks of meloxicam tablets and other treatment options before choosing the appropriate dosage form of meloxicam for a patient. If the benefits outweigh the risks, once-daily dosing is generally preferred. The risk of adverse effects is increased in patients who receive a dosage form of meloxicam with a shorter half-life.

4.2 Alcohol Use

Meloxicam is not contraindicated in patients who use alcohol. The use of alcohol on a regular basis should be avoided in patients who are taking a dosage form of meloxicam with a shorter half-life.

Gastrointestinal Bleeding, Ulceration, and Perforation

NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events compared to non-aspirin NSAIDs. These events can occur at any time during use and without warning symptoms. Increased risk of GI bleeding, ulceration, and perforation with concomitant use of corticosteroids or aspirin with NSAIDs. Use of NSAIDs in patients on warfarin therapy may increase the risk of warfarin-related bleeding events.

Warnings and Precautions, Heart Failure and Edema

Avoid use of meloxicam in patients with severe heart failure.

Warnings and Precautions, Cardiovascular Thrombotic Events

NSAIDs can increase the risk of cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. Avoid use of meloxicam in patients with active peptic ulcer disease and/or GI bleeding who are also taking a dosage form of meloxicam with a shorter half-life.

Dosage and Administration, Juvenile Rheumatoid Arthritis (JRA) Pauciarticular and Polyarticular Course

For the relief of the signs and symptoms of osteoarthritis the recommended starting and maintenance dose is 7.5 mg once daily.

1 INDICATIONS AND USAGE

Meloxicam Tablets are non-steroidal anti-inflammatory drug indicated for:

- Osteoarthritis (OA) (1.1)
- Juvenile Rheumatoid Arthritis (JRA) Pauciarticular and Polyarticular Course (2.4)
- Rheumatoid Arthritis (2.5)
- Ankylosing Spondylitis (2.6)
- Juvenile Spondyloarthritis (2.6)

2 DOSAGE AND ADMINISTRATION

1.1 Osteoarthritis (OA)

The recommended starting and maintenance dose is 7.5 mg once daily.

2.4 Juvenile Rheumatoid Arthritis (JRA) Pauciarticular and Polyarticular Course

The recommended starting and maintenance dose is 7.5 mg once daily.

2.5 Renal Impairment

The recommended starting and maintenance dose is 7.5 mg once daily.

2.6 Non-Interchangeability with Other Formulations of Meloxicam

Meloxicam tablets are non-steroidal anti-inflammatory drug indicated for:

- Osteoarthritis (OA) (1.1)
- Juvenile Rheumatoid Arthritis (JRA) Pauciarticular and Polyarticular Course (2.4)

Not for use in children under the age of 16 years.
Meloxicam is an orally administered, nonsteroidal anti-inflammatory drug (NSAID) with a chemical structure similar to that of other NSAIDs. Meloxicam is approved for the treatment of osteoarthritis and rheumatoid arthritis. Due to its metabolic properties, meloxicam is not subject to hepatic drug metabolism, ensuring its high plasma concentration and absorption rate. It is also characterized by a low gastric irritation index, which makes it suitable for treatment in patients at risk of gastrointestinal damage.

**5.12 Masking of Inflammation and Fever**

5.14 Premature Closure of Fetal Ductus Arteriosus

5.15 Hepatotoxicity

5.16 GI Bleeding, Ulceration, and Perforation

**5.17 Cardiovascular Thrombotic Events**

5.18 Renal Toxicity

5.19 Hematologic Disorders

5.20 Other Important Laboratory Abnormalities

5.22 Pregnancy

5.24 Lactation

5.26 Use in Specific Populations

5.27 Drug Interactions

5.28 Adverse Reactions

5.29 Overdosage

5.30 Carcinogenesis, Mutagenesis, Impairment of Fertility

5.31 Human Pharmacology

**5.32 Post-MI Patients**

Post-MI Patients

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 or CV death, in COX-2 selective-treated patients and nonselective NSAID-treated patients compared to placebo-treated patients. These trials also included patients with a prior history of CV disease.

**5.33 Safe Use in Post-MI Patients**

COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery

Clinical trials of a COX-2 selective NSAID, meloxicam, have shown an approximately two-fold increase in hospitalizations for heart failure in COX-2 selective-treated patients and nonselective NSAID-treated patients compared to placebo-treated patients. This increase in CV deaths has been observed at all doses of meloxicam. These findings are consistent with increased CV risk observed in post-MI patients treated with COX-2 selective NSAIDs and those treated with nonselective NSAIDs.

**5.34 Children**

The safety and effectiveness of meloxicam in children have not been established. Therefore, meloxicam should not be used in children.

**5.35 Pregnancy**

Meloxicam is generally contraindicated in pregnancy. However, in pregnant women who require treatment with meloxicam, the potential benefits of the drug should be weighed against the potential risks.

**5.36 Lactation**

Meloxicam is not recommended for use during lactation due to the potential risk of adverse reactions in the nursing infant.

**5.37 Use in Specific Populations**

In elderly patients, meloxicam may require lower doses due to the risk of renal impairment. Therefore, dosage adjustments may be necessary to avoid the risk of serious renal toxicity.

**5.38 Drug Interactions**

Meloxicam is not recommended in patients who are taking aspirin or other NSAIDs, including any other COX-2 selective NSAID. The combination of meloxicam and an aspirin should be avoided.

**5.39 Adverse Reactions**

Meloxicam is generally well-tolerated, and adverse reactions are usually mild and transient.

**5.40 Overdosage**

In case of overdose, supportive and symptomatic treatment should be provided. Gastric lavage or activated charcoal may be considered if the patient is symptomatic and has ingested a significant amount of meloxicam.

**5.41 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Meloxicam has not been shown to have any carcinogenic, mutagenic, or impairs the fertility of human patients.
recognized pregnancies, regardless of drug exposure, have a background rate of 2-4% for major

second trimesters of pregnancy are inconclusive. In the general U.S. population, all clinically

There are no adequate and well-controlled studies of meloxicam in pregnant women. Data from

Use of NSAIDs, including meloxicam, during the third trimester of pregnancy increases the risk of

Precautions

6.2 Postmarketing Experience

Clinical trials involving approximately 16,200 patients.

Rash was reported in seven (<2%) patients receiving meloxicam. No unexpected adverse

abdominal pain, vomiting, diarrhea, headache, and pyrexia, were more common in the pediatric than in

serious GI events; therefore, the daily dose of meloxicam should not exceed 15 mg.

Higher doses of meloxicam (22.5 mg and greater) have been associated with an increased risk of

Table 1b. Adverse Events (%) Occurring in ≥ 2% of MELOXICAM Patients in two 12-Week

who presented the data below.

The following table lists adverse events occurring in ≥1% of patients receiving meloxicam,

Table 2. Clinical Significance of Drug Interactions with Meloxicam

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<th>Medication</th>
<th>Interaction Type</th>
<th>Clinical Significance</th>
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<tbody>
<tr>
<td>Diclofenac</td>
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<tr>
<td>Methotrexate</td>
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<td>Significant</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Drug Interaction</td>
<td>Significant</td>
</tr>
</tbody>
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Concomitant use of meloxicam and pemetrexed may increase the risk of pemetrexed-associated myelosuppression, renal, and GI toxicity (see the pemetrexed prescribing information). The concomitant use of meloxicam with other NSAIDs or salicylates is not recommended. During concomitant use of meloxicam and cyclosporine, monitor patients for signs of worsening renal function. During concomitant use of meloxicam and lithium, monitor patients for signs of lithium toxicity. When these drugs are administered concomitantly, patients should be adequately hydrated. Assess renal function at the beginning of the concomitant treatment and periodically thereafter.

Concomitant use of meloxicam and low dose aspirin or analgesic doses of aspirin is not generally recommended because of the increased risk of bleeding


table 1: clinical significance of drug interactions with meloxicam
Elderly males (≥ 65 years of age) exhibited meloxicam plasma concentrations and steady-state using AUC values normalized to a dose of 0.25 mg/kg. The elderly patients had meloxicam concentrations ranging from 5 to 15 μg/mL, which are comparable to those found in children (7 to 16 years old). The older patients had a slower elimination rate, with a mean elimination half-life (t½) ranging from 15 hours to 20 hours. The elimination half-life is influenced by age, body mass index (BMI), and renal function.

Meloxicam is extensively metabolized in the liver. Meloxicam metabolites include 5'-carboxy, hydroxymethyl, and 2'-hydroxymetabolites, respectively. There is significant biliary and/or enteral excretion of meloxicam in the feces (1.6%). The extent of the urinary excretion was confirmed for unlabeled multiple 7.5 mg doses: 5% for 24 hours. Meloxicam excretion is predominantly in the form of metabolites, and occurs to equal extents in the urine and feces.

Meloxicam (60% of dose), from P-450 mediated metabolism formed by oxidation of an intermediate. Meloxicam is an inhibitor of prostaglandin synthesis, its mode of action may be due to a decrease in the levels of prostaglandins. Meloxicam is a potent inhibitor of prostaglandin synthesis. The mechanism of action of meloxicam, like that of other NSAIDs, is not completely understood but is thought to involve the inhibition of cyclooxygenase enzymes. Meloxicam concentrations in synovial fluid, after a single oral dose, range from 40% to 50% of those in plasma. Meloxicam concentrations increased with increasing doses up to 15 mg, but then plateaued at 20 mg daily doses. Absorption of meloxicam is rapid and complete after oral administration in fasted subjects. Absorption of meloxicam is not substantially affected by high-fat conditions.

In clinical trials, meloxicam was shown to be bioequivalent to meloxicam tablets. Meloxicam oral suspension doses of 7.5 mg/5 mL and 15 mg/10 mL have been found to be bioequivalent to meloxicam tablets. Absorption of meloxicam was slightly less than that of the tablets, with mean percent bioavailability of 80% and 85% for 7.5 mg and 15 mg, respectively.

The safety and effectiveness of meloxicam in pediatric JRA patients from 2 to 17 years of age has been demonstrated. Meloxicam is indicated for the management of moderate to severe pain in pediatric JRA patients from 2 to 17 years of age. 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 significantly metabolized in the liver and hepatotoxicity may occur, use meloxicam with caution in patients with severe hepatic 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.

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Nonsteroidal Anti-inflammatory Drugs (NSAIDs)?

Medication Guide for Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Zydus Pharmaceuticals USA Inc.

Manufactured by:

Please address medical inquiries to, (MedicalAffairs@zydususa.com) Tel.: 1-877-993-8779.

*Kayexalate is a registered trademark of Sanofi-Aventis

Inform patients not to use low-dose aspirin concomitantly with meloxicam until they talk to their healthcare provider because of the risk of the premature closing of the fetal ductus arteriosus [see Warnings and Precautions (5.2)].

Female Fertility

Advise patients to stop meloxicam immediately if they develop any type of rash and to contact their healthcare provider.

Inform patients of the signs of an anaphylactic reaction (e.g., difficulty breathing, swelling of the face, lips, or tongue) and to contact their healthcare provider if they experience these symptoms.

Anaphylactic Reactions

Advise patients to be alert for the symptoms of congestive heart failure including shortness of breath, weakness, or slurring of speech, and to report any of these symptoms to their healthcare provider.

Heart Failure and Edema

Advise the patient to read the FDA-approved patient labeling (Medication Guide) that accompanies each prescription container of meloxicam and to read it carefully before you start meloxicam therapy and each time you receive a refill so you know what you are taking, how it should be used, the conditions for which it is prescribed, its side effect profile, and appropriate patient monitoring. If you or your patient have any questions about the Medication Guide or meloxicam therapy, contact Zydus at 1-877-993-8779.

Gastrointestinal Bleeding, Ulceration, and Perforation

Advise patients to stop meloxicam and seek immediate medical therapy if they develop gastrointestinal bleeding or perforation, which can be fatal. Patients should be instructed to report any signs and symptoms of bleeding such as hematemesis, melena, or overt gastrointestinal bleeding.

The risk of serious gastrointestinal adverse events (including bleeding, ulceration, and perforation) is greatest with treatment initiation or dosage increase.

Mild to moderate upper gastrointestinal symptoms should be managed with over-the-counter measures for symptomatic relief, such as antacids, H2-receptor antagonists, or proton pump inhibitors. For patients with severe symptoms, a corticosteroid should be used with careful monitoring for appropriate indication.

If the patient's symptoms worsen, if bleeding occurs, or if perforation is suspected, meloxicam should be discontinued and appropriate medical therapy should be initiated.

The risk of serious gastrointestinal adverse events may be lessened by initiation of meloxicam in lower doses in patients with a history of gastrointestinal complications, but the risk of serious adverse events remains.

The risk of serious gastrointestinal adverse events may also be lessened by avoiding initiation of meloxicam in patients with a history of serious gastrointestinal complications when other agents are appropriate.
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)?

Inflammation is a normal response of the body to injury. It is a process that helps to prevent or limit the spread of injury and infection within the body. Inflammation can cause pain, redness, swelling, heat, and stiffness. NSAIDs are medicines that can reduce inflammation without weakening the body's immune system. NSAIDs work by blocking the release of certain natural chemicals that cause inflammation and pain. This is called anti-inflammatory activity. NSAIDs can reduce pain and decrease swelling, redness, and tenderness. NSAIDs are used to treat bone and joint pain caused by conditions such as osteoarthritis, rheumatoid arthritis, gout, tendinitis, bursitis, soft tissue injuries, and sprains. They are also used to treat chronic pain caused by medical conditions such as cancer, inflammatory bowel disease, and inflammatory skin disease. NSAIDs are also used to reduce pain and inflammation caused by surgery, dental procedures, and dental care.

What is the most important information I should know about medicines called NSAIDs?

General information about the safe and effective use of NSAIDs

See "What is the most important information I should know about medicines called NSAIDs?" for a summary of the essential information about medicines called NSAIDs.

How should I take this medicine?

Measures to reduce the risk of bleeding

See "How should I take this medicine?" for a summary of the essential information about medicines called NSAIDs.

When can I expect the medicine to work?

See "When can I expect the medicine to work?" for a summary of the essential information about medicines called NSAIDs.

When should I not take this medicine?

See "When should I not take this medicine?" for a summary of the essential information about medicines called NSAIDs.

What other medicines should I not take with this medicine?

See "What other medicines should I not take with this medicine?" for a summary of the essential information about medicines called NSAIDs.

Who should not take this medicine?

See "Who should not take this medicine?" for a summary of the essential information about medicines called NSAIDs.

What are the side effects of this medicine?

See "What are the side effects of this medicine?" for a summary of the essential information about medicines called NSAIDs.

How should I store this medicine?

See "How should I store this medicine?" for a summary of the essential information about medicines called NSAIDs.

Who is responsible for the information in the Medication Guide? Zydus Pharmaceuticals USA Inc.

What is Zydus Pharmaceuticals USA Inc.?

Zydus Pharmaceuticals USA Inc. is responsible for the information in this Medication Guide. Your doctor or pharmacist can provide you with information about the most important information that applies to your medical situation.

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

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You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or healthcare provider for information about NSAIDs. You can ask your pharmacist or health
### Marketing Information

**Marketing Category**: ANDA

**Application Number or Monograph Citation**: ANDA077921

**Marketing Start Date**: 07/19/2006

**Marketing End Date**: 07/19/2006

### Product Information

**Product Type**: HUMAN PRESCRIPTION DRUG

**Labeler**: Zydus Pharmaceuticals (USA) Inc.

**Registrant**: Zydus Pharmaceuticals (USA) Inc.

**Establishment**: CADILA HEALTHCARE LIMITED

**Product Characteristics**

- **Color**: YELLOW
- **Score**: no score
- **Shape**: ROUND
- **Size**: 8mm
- **Flavor**: Imprint Code: ZC;26

**Contains**:

- MELOXICAM

### Packaging

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