



For Healthcare Professionals only

# Micam

(Meloxicam)

7.5mg and 15mg  
Tablets

میکسیم  
۵۰۰ ملی گرام اور ۱۵۰ ملی گرام  
ٹیبلٹس  
(میلوکسیم)

#### WARNING: CARDIOVASCULAR AND GASTROINTESTINAL RISKS

##### Cardiovascular Events

NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. It is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

##### Gastrointestinal Events

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.

#### QUALITATIVE AND QUANTITATIVE COMPOSITION:

##### **Micam 7.5mg Tablets**

Each tablet contains:  
Meloxicam BP.....7.5mg  
(Product specs: BP)

##### **Micam 15mg Tablets**

Each tablet contains:  
Meloxicam BP.....15mg  
(Product specs: BP)

#### PHARMACEUTICAL FORM

Tablets

#### CLINICAL PARTICULARS

##### **Therapeutic indications**

Micam tablet is indicated for:

- Symptomatic treatment of painful osteoarthritis (arthrosis, degenerative joint disease).
- Symptomatic treatment of rheumatoid arthritis.
- Juvenile Rheumatoid Arthritis (JRA) in patients who weigh  $\geq 60$ kg.

In patients for whom longer-term use may be required, treatment efficacy should be reviewed within the first month of treatment and withdrawn if there is a lack of therapeutic benefit.

Patients on long-term treatment should be reviewed regularly, such as every

three months with regards to efficacy, risk factors and the ongoing need for treatment.

The decision to prescribe a selective COX-2 inhibitor should only be made after assessment of the individual patient's overall risk for developing severe adverse events e.g. history of cardiovascular, renal or gastrointestinal disease, and after use of alternative therapies such as non-pharmacological interventions and simple analgesic therapy where these have been found to lack analgesic efficacy or to have unacceptable adverse effects.

##### **Posology and method of administration**

**Posology:** The total daily should be administered as a single dose. The maximum recommended daily dose is 15mg.

**Painful Osteoarthritis:** 7.5mg/day. If necessary, the dose may be increased to 15mg/day.

**Rheumatoid arthritis:** 15mg/day. According to the therapeutic response, the dose may be reduced to 7.5mg/day.

##### **Special populations**

In patients with an increased risk of adverse reactions e.g. a history of gastrointestinal disease or risk factors for cardiovascular disease, the treatment should be started at a dose of 7.5mg/day.

##### **Renal impairment**

No dose reduction is required in patients with mild or moderate renal impairment (i.e. in patients with a creatinine clearance of greater than 25mL/min). In non-dialyzed patients with severe renal impairment it is contraindicated. In patients with end-stage renal failure on hemodialysis the maximum daily dose should not exceed 7.5mg per day.

##### **Pediatric population**

The maximum recommended daily dose for adolescents aged 12 to 18 years is 0.25mg/kg and should not exceed 15mg. It is contraindicated in children below 12 years of age because the strengths of the dosage forms do not allow appropriate dosing in this age group.

##### **Method of Administration**

Micam tablets are swallowed with water or other fluid in conjunction with food.

## **Contraindications**

- Hypersensitivity to meloxicam.
- Use in patients who have developed signs of asthma, nasal polyps, angioedema or urticaria following the administration of aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs) because of a potential for cross sensitivity.
- Active or recent gastrointestinal ulceration/perforation.
- Active inflammatory bowel disease (Crohn's disease or ulcerative colitis).
- Severe hepatic insufficiency.
- Non-dialyzed severe renal insufficiency.
- Overt gastrointestinal bleeding, recent cerebrovascular bleeding or established systemic bleeding disorders.
- Severe uncontrolled heart failure.
- Patients who have previously had a myocardial infarction or stroke.
- Peri-operative pain in the setting of cardiac surgery, including coronary artery bypass graft (CABG), or major vascular surgery.
- Use in children below 12 years of age.
- Pregnancy or lactation.

## **Special warnings and precautions for use**

### Gastrointestinal effects

Caution should be exercised when treating patients with a history of upper gastrointestinal disease.

Patients with gastrointestinal symptoms should be monitored. It should be withdrawn if gastrointestinal ulceration or bleeding occurs.

As with other NSAIDs, caution should be exercised in patients receiving treatment with anticoagulants. Caution is advised in patients most at risk of developing a gastrointestinal complication with NSAIDs: the elderly, patients using any other NSAID or aspirin concomitantly or patients with a prior history of or recent gastrointestinal disease such as ulceration and gastrointestinal bleeding.

NSAIDs should be prescribed with caution in patients with a prior history of or recent ulcer disease or gastrointestinal bleeding. For high-risk patients, alternate therapies that do not involve NSAIDs should be considered. Minor upper GI problems, such as dyspepsia, are common and may occur at any time during NSAID therapy.

### Cardiovascular and cerebrovascular effects

NSAIDs may increase the risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use.

Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. Use of COX-2 inhibitors (of which meloxicam is one) has been associated with an increased risk of cardiovascular adverse events (myocardial infarction and stroke). This association has been demonstrated with agents of the Coxib class.

Caution is advised in patients with (possible or potential) increased risks when prescribing meloxicam for patients at high risk of cardiovascular adverse events (including patients with diabetes, ischemic heart disease, cardiac failure, hyperlipidemia, hypertension or smokers).

Concurrent use of aspirin negates most of the gastrointestinal benefit associated with COX-2 inhibitors, including meloxicam.

### Skin reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs. It should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

### Renal function

NSAIDs inhibit the synthesis of renal prostaglandins which play a supportive role in the maintenance of renal perfusion.

Patients at greatest risk of such a reaction are elderly individuals, dehydrated patients, those with congestive heart failure, liver cirrhosis, nephrotic syndrome and overt renal disease, those receiving concomitant treatment with a diuretic, ACE inhibitor or angiotensin II receptor antagonist or those having undergone major surgical procedures, which led to hypovolemia, in such patients, the renal function, including the volume of diuresis, should be carefully monitored at the beginning of therapy. In rare instances, NSAIDs may be the cause of interstitial nephritis, glomerulonephritis, renal medullary necrosis or nephrotic syndrome.

The dose in patients with end-stage renal failure on hemodialysis should not exceed 7.5mg. No dose reduction is required in patients with mild or moderate renal impairment (i.e. in patients with a creatinine clearance of greater than 25mL/min).

### Liver function

As with most other NSAIDs, occasional elevations of serum transaminases and other parameters of liver function have been reported.

If the abnormality is significant or persistent, it should be stopped and follow up tests carried out. No dose reduction is required in patients with clinically stable liver cirrhosis.

### Sodium, potassium and water retention

Induction of sodium, potassium and water retention and interference with the natriuretic effects of diuretics may occur with NSAIDs. Use of COX-2 inhibitors or other NSAIDs may precipitate or exacerbate pre-existing hypertension, cardiac failure or edema in susceptible patients, and the treatment of these conditions may be compromised.

### Other warnings and precautions

As with other NSAIDs, caution should be used in the treatment of elderly patients who are more likely to be suffering from impaired renal, hepatic or cardiac function. Meloxicam, like any other NSAID, may mask symptoms of an underlying infectious disease. Women who have difficulties in conceiving withdrawal should be considered.

This medicinal product contains lactose. Patients with rare hereditary conditions of galactose intolerance, e.g. galactosaemia, should not take this medicine.

### Interaction with other medicinal products and other forms of interaction Other Prostaglandin Synthetase Inhibitors (PSI) including glucocorticoids and salicylates (acetylsalicylic acid)

Co-administration of PSIs may increase the risk of gastrointestinal ulcers and bleeding, via a synergistic effect, and is not recommended. The concomitant use of meloxicam with other NSAIDs is not recommended.

### Oral anticoagulants, systemically administered heparin, thrombolytics

Increased risk of bleeding. If such co-prescribing cannot be avoided, close monitoring of their effects on coagulation is required.

### Antiplatelet drugs and Selective Serotonin Reuptake Inhibitors (SSRIs)

Increased risk of bleeding via inhibition of platelet function.

### Diuretics

Treatment with NSAIDs is associated with the potential for acute renal insufficiency in patients who are dehydrated. Patients receiving meloxicam

and diuretics should be adequately hydrated and be monitored for renal function prior to initiating treatment.

#### Antihypertensives (e.g. beta-blockers, ACE-inhibitors, vasodilators, diuretics)

A reduced effect of the antihypertensive drug by inhibition of vasodilating prostaglandins has been reported during treatment with NSAIDs. In patients with pre-existing renal impairment this may lead to acute renal failure.

#### Calcineurin inhibitors

Nephrotoxicity of cyclosporine may be enhanced by NSAIDs via renal prostaglandin mediated effects. During combined treatment renal function is to be measured.

#### Contraception

A decrease of the efficacy of intrauterine devices by NSAIDs has been previously reported but needs further confirmation.

#### Lithium

The concomitant use of lithium and NSAIDs is not recommended. If this combination appears necessary, lithium plasma concentrations should be monitored carefully during the initiation, adjustment and withdrawal of meloxicam treatment.

#### Methotrexate

NSAIDs can reduce the tubular secretion of methotrexate thereby increasing the plasma concentrations of methotrexate. For this reason, for patients on high dosages of methotrexate (more than 15mg/week) the concomitant use of NSAIDs is not recommended.

Caution should be taken in case both NSAID and methotrexate are given within 3 days, in which case the plasma level of methotrexate may increase and cause increased toxicity. It should be considered that the hematological toxicity of methotrexate can be amplified by treatment with NSAID drugs.

#### Pemetrexed

For the concomitant use of meloxicam with pemetrexed in patients with creatinine clearance from 45 to 79mL/min, the administration of meloxicam should be paused for 5 days before, on the day of, and two days following pemetrexed administration. If a combination of meloxicam with pemetrexed is necessary, patients should be closely monitored, especially for myelosuppression and gastrointestinal adverse reactions. In patients with creatinine clearance below 45mL/min the concomitant administration of meloxicam with pemetrexed is not recommended.

#### Cholestyramine

Binds meloxicam in the gastrointestinal tract leading to a faster elimination of meloxicam. Interactions via CYP 2C9 can be expected in combination with medicinal products such as oral antidiabetics (sulphonylureas, nateglinide), which may lead to increased plasma levels of these drugs and meloxicam.

Patients concomitantly using meloxicam with sulphonylureas or nateglinide should be carefully monitored for hypoglycemia. No relevant pharmacokinetic drug-drug interactions were detected with respect to the concomitant administration of antacids, cimetidine, digoxin and furosemide.

#### Fertility, Pregnancy and Lactation

Fertility: It may impair fertility and is not recommended in women attempting to conceive.

Pregnancy: Inhibition of prostaglandin-synthesis may adversely affect pregnancy and/or the embryo-fetal development. It is contraindicated during pregnancy.

Lactation: NSAIDs are known to pass into mother's milk. Administration therefore is contraindicated in women who are breastfeeding.

#### **Effects on ability to drive and use machines**

It is not likely to affect the ability to drive or use machines. Adverse drug reactions such as dizziness and visual disturbances may occur. If affected, patients should not drive or operate machinery.

#### **Undesirable effects**

Adverse reactions listed below are classified according to frequency and System Organ Class (SOC). Frequency categories are defined according to the following convention: Very common (≥ 1/10), Common (≥ 1/100 to < 1/10), Uncommon (≥ 1/1,000 to < 1/100), Rare (≥ 1/10,000 to < 1/1,000), Very rare (< 1/10,000), Not known

System organ class	Adverse reaction	Frequency
<b>Blood and lymphatic system disorders</b>	Anemia	Uncommon
	Blood count abnormal (including differential white cell count), leukopenia, thrombocytopenia	Rare
<b>Immune system disorders</b>	Other immediate hypersensitivity	Uncommon
	Anaphylactic reaction, anaphylactoid reaction.	Not known
<b>Psychiatric disorders</b>	Mood altered	Rare
	state of Confusion, disorientation	Not known
<b>Neurotic system disorders</b>	Headache	Common
	Dizziness, somnolence	Uncommon
<b>Eye disorders</b>	Blurred vision, conjunctivitis	Rare
	Vertigo	Uncommon
<b>Ear and labyrinth disorders</b>	Tinnitus	Rare
	Palpitations	Rare
<b>Cardiac disorder</b>	palpitations	Rare
<b>Vascular disorder</b>	blood pressure increased, flushing	Uncommon
<b>Respiratory, thoracic &amp; mediastinal disorders</b>	Asthma in individuals allergic to aspirin or other NSAIDs.	Rare
	Abdominal pain, dyspepsia, diarrhoea, nausea, vomiting	Common
<b>Gastrointestinal disorders</b>	Occul or macroscopic gastrointestinal haemorrhage, gastritis, stomatitis, constipation, flatulence, eructation	Common
	Gastro duodenal ulcer, colitis, esophagitis	Rare
	Gastrointestinal perforation	Very rare
	Liver function test abnormal (e.g. raised transaminases or bilirubin)	Uncommon
<b>Hepatobiliary disorders</b>	Hepatitis	Very rare
	Angioedema, rash, pruritus	Uncommon
<b>Skin and subcutaneous tissue disorders</b>	Toxic epidermal necrolysis, Stevens-Johnson syndrome, urticaria	Rare
	Dermatitis bullous, erythema multiforme	Very rare
	Photosensitivity reaction	Not known
	Renal function test abnormal (increased serum creatinine and/or serum urea), micturition disorders, including acute urinary retention	Uncommon
<b>Renal and urinary disorders</b>	Renal failure acute	Very rare
	Infertility female	Not known
<b>Reproductive system and breast disorders</b>	Infertility female	Not known
<b>Endocrine disorders</b>	Ovulation delayed	Uncommon
	Edema	Uncommon
<b>General disorders</b>	Edema	Uncommon

#### **Overdose**

General symptomatic treatment includes standard measures of gastric evacuation and supportive measures are indicated as required.

### **PHARMACOLOGICAL PROPERTIES**

#### **Pharmacodynamic Properties**

Pharmacotherapeutic group: Anti-inflammatory and Anti-rheumatic products, Non-steroids, Oxicans.

ATC code: M01AC06

#### Mechanism of action

Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the enolic acid class. Meloxicam showed potent anti-inflammatory activity in all standard models of inflammation. A common mechanism for the above effects may exist in the ability of meloxicam to inhibit the biosynthesis of prostaglandins, known mediators of inflammation.

## Pharmacokinetic Properties

### Absorption

Oral administration: Meloxicam is well absorbed from the gastrointestinal tract, which is reflected by a high absolute bioavailability of about 90% following oral administration. Following single dose administration of meloxicam, median maximum plasma concentrations are achieved within 5-6 hours for the tablets.

Extent of absorption for meloxicam following oral administration is not altered by concomitant food intake or the use of inorganic antacids. Mean maximum plasma concentrations of meloxicam at steady state, are achieved within five hours for the tablet.

### Distribution

Meloxicam is very strongly bound to plasma proteins, essentially albumin (99%). Meloxicam penetrates into synovial fluid to give concentrations approximately half of those in plasma. Volume of distribution is low, i.e. approx. 11L. Extent of absorption for meloxicam following oral administration is not altered by concomitant food intake or the use of inorganic antacids.

### Biotransformation

Meloxicam undergoes extensive hepatic biotransformation. Four different metabolites of meloxicam were identified in urine, which are all pharmacodynamically inactive. The major metabolite, 5'-carboxymeloxicam (60% of dose), is formed by oxidation of an intermediate metabolite 5'-hydroxymethylmeloxicam, which is also excreted to a lesser extent (9% of dose).

### Elimination

Meloxicam is excreted predominantly in the form of metabolites and occurs to equal extents in urine and feces. Less than 5% of the daily dose is excreted unchanged in feces, while only traces of the parent compound are excreted in urine. The mean elimination half-life varies between 13 and 25 hours after oral IM and IV administration. Total plasma clearance amounts to about 7-12mL/min following single doses orally, intravenously or rectally administered.

### Special populations

Patients with hepatic/renal insufficiency: Neither hepatic insufficiency, nor mild renal insufficiency has a substantial effect on meloxicam pharmacokinetics. In terminal renal failure a daily dose of 7.5mg must not be exceeded.

## PHARMACEUTICAL PARTICULARS

### Incompatibilities

Not applicable

## Shelf life

03 years

## Special precautions for storage and instructions

Protect from heat, sunlight & moisture, store below 25°C. The expiration date refers to the product correctly stored at the required condition. Keep out of the reach of children.

To be sold on the prescription of a registered medical practitioner only.  
"Product contains lactose"

## Nature and contents of container/presentation

MICAM 7.5mg Tablets: Cold form & Cold seal Alu Alu blister pack of 10 Tablets  
MICAM 15mg Tablets: Cold form & Cold seal Alu Alu blister pack of 10 Tablets

## REGISTRATION HOLDER / MARKETING AUTHORIZATION HOLDER Head Office:

Bosch Pharmaceuticals (Pvt.) Ltd  
8, Modern society Tipu Sultan Road, Karachi-Pakistan

## Manufacturer:

Bosch Pharmaceuticals (Pvt.) Ltd.,  
Plot No. 221-223, Sector 23, Korangi Industrial area, Karachi-Pakistan

## REGISTRATION / MARKETING AUTHORIZATION NUMBER

Micam 7.5mg Tablets: 044037  
Micam 15mg Tablets: 044038

## DATE FROM WHICH MARKETING IS AUTHORIZED/RENEWAL OF THE AUTHORIZATION

Micam 7.5mg Tablets: 11-09-2006/10-09-2021  
Micam 15mg Tablets: 11-09-2006/10-09-2021

## DATE OF REVISION OF THE TEXT

20-05-2024

ہدایات:-

دھوپ، گرمی اور نمی سے محفوظ ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔  
بچوں کی پہنچ سے دور رکھیں۔

صرف مسترد ڈاکٹر کے نسخے پر فروخت کے لئے۔



Manufactured by:

**Bosch Pharmaceuticals (Pvt.) Ltd.**

221-223, Sector 23, Korangi Industrial Area,  
Karachi - Pakistan

