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Melor® Tablets
(Meloxicam)

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

Cardiovascular Risk: Nonsteroidal anti-inflammatory drugs (NSAIDs) may cause an increased risk of serious cardiovascular (CV) 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. Meloxicam is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery
Gastrointestinal Risk: NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse reactions 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

Melor® 7.5mg Tablets
Each tablet contains:
Meloxicam BP.....7.5mg

Melor® 15mg Tablets
Each tablet contains:
Meloxicam BP.....15mg

PHARMACEUTICAL FORM
Tablet

CLINICAL PARTICULARS
THERAPEUTIC INDICATIONS:
- Short-term symptomatic treatment of exacerbations of osteoarthrosis.
- Long-term symptomatic treatment of rheumatoid arthritis or ankylosing spondylitis.
- Melor® tablets are indicated in adults and children aged 16 years and older.

POSOLOGY AND METHOD OF ADMINISTRATION:
Posology:
- The total daily amount should be taken as a single dose.
- Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically, especially in patients with osteoarthritis.
- ***Exacerbations of osteoarthrosis:*** 7.5mg/day. If necessary, in the absence of improvement, the dose may be increased to 15mg/day.
- ***Rheumatoid arthritis, ankylosing spondylitis:*** 15mg/day. According to the therapeutic response, the dose may be reduced to 7.5mg/day.
- Do not exceed the dose of 15mg/day.

SPECIAL POPULATIONS:
Elderly patients: The recommended dose for long term treatment of rheumatoid arthritis and ankylosing spondylitis in elderly patients is 7.5mg per day.
Patients with increased risks for adverse reaction: In patients with increased risks for adverse reactions, e.g. a history of gastro-intestinal disease or cardiovascular disease, the treatment should be started at a dose of 7.5mg per day.
Renal impairment: Contraindicated in non-dialyzed severe renal failure. In patients with end-stage renal failure on haemodialysis, the dose should not exceed 7.5mg per day. No dose reduction is required in patients with mild to moderate renal impairment (i.e. patients with a creatinine clearance of greater than 25ml/min).
Hepatic impairment: No dose reduction is required in patients with mild to moderate hepatic impairment.
Paediatric population: Contraindicated in children and adolescents below 16 years of age.

Method of administration:
For oral use. Melor® tablets are swallowed with water or other fluid in conjunction with food.

CONTRAINDICATIONS:
- Hypersensitivity to the active substance or substances with a similar action, e.g. non-steroidal anti-inflammatory drugs (NSAIDs), aspirin.
- Third trimester of pregnancy.
- Children and adolescents below 16 years of age.
- Patients who have developed signs of asthma, nasal polyps, angio-edema or urticaria following the administration of aspirin or other NSAIDs.
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.
- Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- Severely impaired liver function.
- Non-dialyzed severe renal failure.
- Gastrointestinal bleeding.
- History of cerebrovascular bleeding or other bleeding disorders.
- Severe heart failure.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:
The use of meloxicam with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided. Meloxicam is not appropriate for the treatment of patients requiring relief from acute pain.
Gastrointestinal effects: The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk. In patients receiving concomitant medications such as heparin as curative treatment or given in geriatrics, warfarin, other non-steroidal anti-inflammatory drugs, or acetylsalicylic acid given at doses ≥500mg as single intake or ≥3g as total daily amount, the combination with meloxicam is not recommended. When GI bleeding or ulceration occurs in patients receiving meloxicam, the treatment should be withdrawn.
Cardiovascular and cerebrovascular effects: Clinical monitoring of blood pressure for patients at risk is recommended at baseline and especially during treatment initiation with meloxicam. Patients with uncontrolled hypertension, congestive heart failure, established ischemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with meloxicam after careful consideration. Appropriate monitoring and advice are required.
Skin reactions: Life-threatening cutaneous reactions Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the use of meloxicam. If symptoms or signs of SJS or TEN are present, meloxicam treatment should be discontinued.
Parameters of liver and renal function: As with most NSAIDs, occasional increases in serum transaminase levels, increases in serum bilirubin or other liver function parameters, as well as increases in serum creatinine and blood urea nitrogen and other laboratory disturbances, the administration of meloxicam should be stopped.
Functional renal failure: Careful monitoring of the renal function including the volume of diuresis is recommended in patients with the following risk factors: Elderly, concomitant treatments such as ACE inhibitors, angiotensin-II antagonists, sartans, diuretics, hypovolemia (whatever the cause), congestive heart failure, renal failure, nephrotic syndrome, lupus nephropathy, severe hepatic dysfunction (serum albumin <25g/l or Child-Pugh score ≥10). The dose of meloxicam in patients with end-stage renal failure on haemodialysis 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 25 ml/min).
Sodium, potassium and water retention: Clinical monitoring is necessary for patients at risk.
Hyperkalaemia: Can be favored by diabetes or concomitant treatment known to increase. Regular monitoring of potassium values should be performed.
Combination with pemetrexed: In patients with mild to moderate renal insufficiency receiving pemetrexed, meloxicam should be interrupted for at least 5 days prior to, on the day of, and at least 2 days following pemetrexed administration.
Other warnings and precautions: The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal. Meloxicam, as any other NSAID may mask symptoms of an underlying infectious disease. The use of meloxicam may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of meloxicam should be considered. Meloxicam tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp-lactase deficiency or glucose-galactose malabsorption should not take this medicine.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTIONS:
Risks related to hyperkalaemia: Potassium salts, potassium-sparing diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists, non-steroidal anti-inflammatory drugs, (low-molecular-weight or unfractionated) heparins, cyclosporin, tacrolimus and trimethoprim. This risk is increased when the above-mentioned medicinal products are co-administered with meloxicam.

Pharmacodynamic interactions: ***Other non-steroidal anti-inflammatory drugs (NSAIDs) and acetylsalicylic acid:*** Combination with other non-steroidal anti-inflammatory drugs, acetylsalicylic acid given at doses ≥ 500mg as single intake or ≥ 3g as total daily amount is not recommended.
Corticosteroids (e.g. Glucocorticoids): The concomitant use with corticosteroids can increase risk of bleeding or gastrointestinal ulceration.
Anticoagulant or heparin: NSAIDs may enhance the effects of anti-coagulants, such as warfarin. The concomitant use of NSAIDs and anticoagulants or heparin administered in geriatrics or at curative dose is not recommended. Careful monitoring of the INR is required if it proves impossible to avoid such combination.
Thrombolytics and antiplatelet drugs: Increased risk of bleeding, via inhibition of platelet function and damage to the gastroduodenal mucosa.
Selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding.
Diuretics, ACE inhibitors and Angiotensin-II Antagonists: Combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.
Other antihypertensive drugs (e.g. Beta-blockers): A decrease of the antihypertensive effect of beta-blockers (due to inhibition of prostaglandins with vasodilatory effect) can occur.
Calcineurin inhibitors (e.g. cyclosporin, tacrolimus): Nephrotoxicity of calcineurin inhibitors may be enhanced by NSAIDs via renal prostaglandin mediated effects. A

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careful monitoring of the renal function is recommended, especially in the elderly.
Deferasirox: The concomitant administration of meloxicam with deferasirox may increase the risk of gastro-intestinal adverse reactions. Caution should be exercised when combining these medicinal products.

Pharmacokinetic interactions: Effect of meloxicam on the pharmacokinetics of other drugs: *Lithium:* The concomitant use of lithium and NSAIDs is not recommended.
Methotrexate: 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.
Pemetrexed: For the concomitant use of meloxicam with pemetrexed in patients with creatinine clearance from 45 to 79 ml/min, the administration of meloxicam should be paused for 5 days before, on the day of, and 2 days following pemetrexed administration. If a combination of meloxicam with pemetrexed is necessary, patients should be closely monitored, especially for myelosuppression and gastro-intestinal adverse reactions. In patients with severe renal impairment (creatinine clearance below 45 ml/min) the concomitant administration of meloxicam with pemetrexed is not recommended. Caution should be exercised when administering 15mg meloxicam concurrently with pemetrexed to patients with normal function (creatinine clearance ≥ 80 ml/min).

Pharmacokinetic interactions: Effect of other drugs on the pharmacokinetics of meloxicam: *Cholestyramine:* Cholestyramine accelerates the elimination of meloxicam by interrupting the enterohepatic circulation so that clearance for meloxicam increases by 50% and the half-life decreases to 13+3 hrs.

Pharmacokinetic interactions: Effect of combination of meloxicam and of other drugs on the pharmacokinetics: *Oral antidiabetics (sulphonylureas, nateglinide):*
Patients concomitantly using meloxicam with sulphonylureas or nateglinide should be carefully monitored for hypoglycaemia.
Paediatric population: Interaction studies have only been performed in adults.

FERTILITY, PREGNANCY AND LACTATION:
Fertility: The use of meloxicam, as with any drug known to inhibit cyclooxygenase/prostaglandin synthesis, may impair female fertility and is not recommended in women attempting to conceive.
Pregnancy: During the first and second trimester of pregnancy, meloxicam should not be given unless clearly necessary. If meloxicam is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Meloxicam is contraindicated during the third trimester of pregnancy.
Breastfeeding: Meloxicam is not recommended in women who are breastfeeding.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Meloxicam is likely to have no or negligible influence on these abilities. However, when visual disturbances including blurred vision, dizziness, drowsiness, vertigo or other central nervous system disturbances occur, it is advisable to refrain from driving and operating machinery.

UNDESIRABLE EFFECTS:
Edema, hypertension, and cardiac failure, have been reported in association with NSAID treatment.
The most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease.
Severe cutaneous adverse reactions (SCARs): Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported.
Blood and lymphatic system disorders: *Uncommon:* Anaemia. ***Rare:*** Blood count abnormal (including differential white cell count), leukopenia, and thrombocytopenia. ***Very rare:*** Agranulocytosis
Immune system disorders: *Uncommon:* Allergic reactions other than anaphylactic or anaphylactoid reactions. ***Not known:*** Anaphylactic reaction, anaphylactoid reaction.
Psychiatric disorders: *Rare:* Mood altered, nightmares. ***Not known:*** Confusional state, disorientation.
Nervous system disorders: *Common:* Headache. ***Uncommon:*** Dizziness, somnolence.
Eye disorders: *Rare:* Visual disturbance including vision blurred; conjunctivitis.
Ear and labyrinth disorders: *Uncommon:* Vertigo. ***Rare:*** Tinnitus.
Cardiac disorders: *Rare:* Palpitations. Cardiac failure has been reported in association with NSAID treatment.
Vascular disorders: *Uncommon:* Blood pressure increased, flushing.
Respiratory, thoracic and mediastinal disorders: Rare: Asthma in individuals allergic to aspirin or other NSAIDs.
Gastrointestinal disorders: *Very common:* Gastrointestinal disorders such as dyspepsia, nausea, vomiting, abdominal pain, constipation, flatulence, and diarrhoea. ***Uncommon:*** Occult or macroscopic gastrointestinal haemorrhage, stomatitis, gastritis, eructation. ***Rare:*** Colitis, gastroduodenal ulcer, esophagitis. ***Very rare:*** Gastrointestinal perforation. ***Not known:*** Pancreatitis. Gastrointestinal haemorrhage, ulceration or perforation may sometimes be severe and potentially fatal, especially in elderly.
Hepatobiliary disorders: *Uncommon:* Liver function disorder (e.g. raised transaminases or bilirubin). ***Very rare:*** Hepatitis.
Skin and subcutaneous tissue disorders: *Uncommon:* Angio-oedema, pruritus, rash. ***Rare:*** Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria.
Very rare: Dermatitis bullous, erythema multiforme. ***Not known:*** Photosensitivity reaction.
Renal and urinary disorders: *Uncommon:* Sodium and water retention, hyperkalaemia, renal function test abnormal (increased serum creatinine and/or serum urea).
Very rare: Acute renal failure in particular in patients with risk factors.
Reproductive system and breast disorders: *Not known:* Infertility female, ovulation delayed.
General disorders and administration site conditions: *Uncommon:* Edema including edema of the lower limbs. ***Very rare:*** Cases of agranulocytosis have been reported in patients treated with meloxicam and other potentially myelotoxic drugs.
Organic renal injury probably resulting in acute renal failure: *Very rare:* cases of interstitial nephritis, acute tubular necrosis, nephrotic syndrome, and papillary necrosis have been reported

OVERDOSE:
Patients should be managed with symptomatic and supportive care following an NSAID overdose. Administration of activated charcoal is recommended for patients who present 1 to 2 hours after overdose, activated charcoal may be administered repeatedly. Administration of cholestyramine may be useful following an overdose.

PHARMACOLOGICAL PROPERTIES
PHARMACODYNAMIC PROPERTIES:
Pharmacotherapeutic group: Anti-Inflammatory and antirheumatic products, non-steroids; Oxicams. **ATC code:** M01AC06.
Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam family, with anti-inflammatory, analgesic and antipyretic properties.

PHARMACOKINETIC PROPERTIES:
Absorption: Meloxicam is well absorbed from the gastrointestinal tract, which is reflected by a high absolute bioavailability of about 90% following oral administration. Extent of absorption for meloxicam following oral administration is not altered by concomitant food intake or the use of inorganic antacids.
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. 11 L after i.m. or i.v. administration, and shows interindividual variation in the order of 7 - 20%. The volume of distribution following administration of multiple oral doses of meloxicam (7.5 to 15mg) is about 16 L with coefficients of variation ranging from 11 to 32%.
Biotransformation: Meloxicam undergoes extensive hepatic biotransformation. Four different metabolites of meloxicam were identified in urine, which are all pharmacodynamically inactive.
Elimination: Meloxicam is excreted predominantly in the form of metabolites and occurs to equal extents in urine and faeces. Less than 5% of the daily dose is excreted unchanged in faeces, while only traces of the parent compound are excreted in urine.

SHELF LIFE
See expiry on the pack.

AVAILABILITY
Melor® 7.5mg tablets in a pack of 20's
Melor® 15mg tablets in a pack of 20's

INSTRUCTIONS
Dosage: As advised by the physician.
To be sold on the prescription of a registered medical practitioner only.
Keep out of the reach of children.
Avoid exposure to heat, light and humidity.
Store between 15 to 30°C.
Improper storage may deteriorate the medicine.

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com
Mfg. Lic. No. 000072

میلور ٹیبلٹ
(میلوکسیکیم)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو گرمی، روشنی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری
سینٹی گریڈ کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی۔

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