Item Code	: 204492 - 03 draft 26 Jan 2024
PM Code	: Ins.P MOT15
Measurement(mm) ± 2mm	: 260(L) x 110(W)
CURSOR (ATTACHMENT 1)	: T 087 - T092 mm
CURSOR (ATTACHMENT 2)	: L 093 - L101 mm
Colour of Artwork	: K 100
Source of Artwork	: MAC 3 / CC

Melocam® Tablet 15mg

Ingredient(s):
Each tablet contains:
Meloxicam 15mg

Pharmacology (Summary of Pharmacodynamic and Pharmacokinetic):
Pharmacodynamic:
Meloxicam is a nonsteroidal anti-inflammatory drug (NSAIDs) of the enolic acid class that has shown anti-inflammatory, analgesic and antipyretic properties in animals. Meloxicam inhibits biosynthesis of prostaglandins, the known mediators of inflammation. Comparison of the ulcerogenic dose and the anti-inflammatory effective dose in the rat adjuvant arthritis confirmed a superior therapeutic margin in animals over standard NSAIDs. The selective inhibition of COX-2 relative to COX-1 by meloxicam has been demonstrated in *vitro* on various cell systems. Clinical studies demonstrated a lower incidence of gastrointestinal adverse events with the recommended doses of meloxicam than standard doses of other NSAIDs.
Pharmacokinetic:
Meloxicam is well absorbed following oral administration (89%). The absorption is not affected by concomitant food intake. Steady-state conditions are achieved in 3-5 days. In plasma, >99% is bound to plasma proteins. Once-daily dosing leads to drug plasma concentrations with a relatively small peak-trough fluctuation in the range of 0.8-2ug/ml for 15.0mg doses (C_{min} and C_{max} at steady state, respectively).
Meloxicam penetrates well into synovial fluid to give concentrations approximately half of those in plasma. Meloxicam is extensively metabolized and <5% of the daily dose is extracted unchanged in faeces, while only traces of the unchanged compound are excreted in the urine. The mean elimination half-life of Meloxicam is 20 hours.
Neither hepatic, nor mild to moderate renal insufficiency does substantially affect Meloxicam pharmacokinetics. Plasma clearance is on average 8mL/min. Clearance is decreased in the elderly. Volume of distribution is low, on average 11L.

Indication(s):
Pain and inflammation in rheumatic disease; exacerbation of osteoarthritis (arthrosis, degenerative joint disease) and ankylosing spondylitis.

Dosage and Administration(s):
Osteoarthritis: 7.5mg daily, increased if necessary up to a maximum of 15mg once daily.
Rheumatoid arthritis: 15mg daily (The dose may be reduced to 7.5mg daily depending on therapeutic response).
Ankylosing spondylitis: 15mg daily
In patients with increased risks of adverse reactions, start with the dose of 7.5mg daily.
In dialysis patients with severe renal failure, the dose should not exceed 7.5mg/day.
The total daily dosage should not exceed 15mg.
The tablets should be taken with water or other fluid in conjunction with food.
After assessing the risk/benefit ratio in each individual patient, the lowest effective dose for the shortest possible duration should be used.
To be taken orally, with water or other fluid in conjunction with food.

Route of Administration: Oral

Contraindication(s):
Active peptic ulceration, severe hepatic insufficiency, non-dialysed severe renal insufficiency, children < 15 years old, hypersensitivity to NSAIDs. Pregnancy and lactation.

Precaution(s) / Warning(s):
1. **Cardiovascular Thrombotic Events.** Observational studies indicated that non-selective NSAIDs may be associated with an increased risk of serious cardiovascular events, principally myocardial infarction, which may increase with dose or duration of use. Patients with cardiovascular disease or cardiovascular risk of an adverse cardiovascular event in patient taking NSAID, especially in those with cardiovascular risk factors, the lowest effective dose should be used for the shortest possible duration. There is no consistent evidence that the concurrent use of aspirin mitigates the possible increased risk of serious cardiovascular thrombotic events associated with NSAID use.
2. **Hypertension.** NSAIDs may lead to the onset of new hypertension or worsening the pre-existing hypertension and patients taking antihypertensive with NSAIDs may have an impaired antihypertensive response. Caution is advised when prescribing NSAIDs to patients with hypertension. Blood pressure should be monitored closely during initiation of NSAID treatment and at regular intervals thereafter.
3. **Heart Failure.** Fluid retention and oedema have been observed in some patients taking NSAIDs, hence caution is advised in patients with fluid retention of heart failure.
4. **Gastrointestinal Events.** All NSAIDs can cause gastrointestinal discomfort and rarely serious, potentially fatal gastrointestinal effects such as ulcers, bleeding and perforation which may increase with dose or duration of use, but can occur at any time without warning. Caution is advised in patients with risk factors for gastrointestinal events e.g. the elderly, those with a history of serious gastrointestinal events, smoking and alcoholism. When gastrointestinal bleeding or ulcerations occur in patients receiving NSAIDs, the drug should be withdrawn immediately. Doctors should warn patient about signs and symptoms of serious gastrointestinal toxicity. The concurrent use of aspirin and NSAIDs also increases the risk of serious gastrointestinal adverse events.
5. **Severe Skin Reactions.** NSAIDs may very rarely cause serious cutaneous adverse events such as exfoliative dermatitis, toxic epidermal necrolysis (TEN) and Stevens-Johnson Syndrome (SJS), which can be fatal and occur without warning. These serious adverse events are idiosyncratic and are independent of dose or duration of use. Patients should be advised of the signs and symptoms of serious skin reactions and to consult their doctor at the first appearance of a skin rash or any other sign of hypersensitivity.
6. **Renal Impairment.** In patients with decreased renal blood flow and blood volume, administration of NSAIDs may precipitate overt renal decompensation which is typically followed by recovery to pre-treatment state upon discontinuation of non-steroidal anti-inflammatory therapy.
7. **Others.** Close monitoring is recommended for patients with dehydration, liver cirrhosis, nephrotic syndrome, overt renal disease, those receiving a diuretic or those having undergone major surgical procedures which led to hypovolaemia, and elderly.
8. Meloxicam should be stopped and follow-up tests carried out if the abnormality elevations of serum transaminases or other parameters of the liver function are significant or persistent.
9. There are no specific studies about effects on the ability to drive vehicles and to use machinery. Patients who experience visual disturbances, drowsiness or other central nervous system disturbances should refrain from these activities.

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WARNINGS
RISK OF GI ULCERATION, BLEEDING
AND PERFORATION WITH NSAID

Serious GI toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated with NSAID therapy. Although minor upper GI problems (eg: dyspepsia) are common, usually developing early in therapy, prescribers should remain alert for ulceration and bleeding in patients treated with NSAID even in absence of previous GI tract symptoms.
Studies to date have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Patients with prior history of serious adverse events and other risk factors associated with peptic ulcer disease (eg: alcoholism, smoking, and corticosteroid therapy) are at increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less than other individuals and account for most spontaneous for fatal GI events.

Interaction with Other Medicaments:
1. Concomitant administration of more than one NSAID may increase the risk of gastrointestinal ulceration and bleeding through synergistic action.
2. Oral anticoagulants, ticlopidine, systemically administered heparin, thrombolytics: Increased risk of bleeding. Close monitoring of the effects of anticoagulants is required.
3. Lithium: Increased lithium plasma levels. It is recommended that plasma lithium levels be monitored when initiating, adjusting and discontinuing Meloxicam.
4. Methotrexate: Meloxicam may increase the hematologic toxicity of methotrexate. Strict monitoring of blood cell count is recommended.
5. Contraception: Decrease the efficacy of intrauterine devices.
6. Diuretics: Patients receiving Meloxicam and diuretics should be adequately hydrated and be monitored for renal function prior initiating treatment.
7. Antihypertensives (eg. β-blockers, ACE inhibitors, vasodilators, diuretics): A reduced effect of the antihypertensive drug by inhibition of vasodilating prostaglandins has been reported during treatment with NSAIDs.
8. Cholestyramine binds Meloxicam in the gastrointestinal tract leading to a faster elimination of Meloxicam.
9. Cyclosporin: Nephrotoxicity may be enhanced by NSAIDs via renal prostaglandin-mediated effects. Renal function is to be measured during combined treatment.
10. No relevant pharmacokinetic drug-drug interactions were detected with respect to the concomitant administration of antacids, cimetidine, digoxin and furosemide. Interactions with oral antidiabetics cannot be excluded.

Pregnancy and Lactation:
Meloxicam is not recommended for pregnant and breast-feeding women.

Side Effect(s):
Gastrointestinal: >1%: Dyspepsia, nausea, vomiting, abdominal pain, constipation, flatulence and diarrhea; 0.1-1%: Transitory abnormalities of liver function parameters (eg. Raised transaminases or bilirubin), eructation, esophagitis, gastro-duodenal ulcer, occult or macroscopic gastrointestinal bleeding; <0.1%: Gastrointestinal perforation, colitis, hepatitis, gastritis
Hematological: >1%: Anemia; 0.1-1%: Disturbances of blood count, including differential white cell count, leucopenia and thrombocytopenia.
Concomitant administration of a potentially myelotoxic drug in particular methotrexate, appears to be a predisposing factor to the onset of cytopenia.
Dermatological: >1%: Pruritus and skin rash; 0.1-1%: Stomatitis and urticaria; <0.1%: Photosensitization. On rare occasions bullous reactions, erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis may develop.
Respiratory: <0.1%: Onset of acute asthma has been reported in certain individuals following NSAIDs including Meloxicam.
Central Nervous System: >1%: lightheadedness and headache; 0.1-1%: Vertigo, tinnitus and drowsiness; <0.1%: Confusion and disorientation.
Cardiovascular: >1%: Oedema; 0.1-1%: Increase of blood pressure, palpitations and flushes.
Genitourinary: 0.1-1%: Abnormal renal function parameters (increased serum creatinine and/or serum urea); <0.1%: Acute renal failure.
Vision Disorders: <0.1%: Conjunctivitis, visual disturbances including blurred vision.
Hypersensitivity Reactions: <0.1%: Angio-oedema and immediate hypersensitivity reactions including anaphylactoid / anaphylactic reactions.

Symptoms and Treatment for Overdosage, and Antidote(s):
The standard measures of gastric evacuation and general supportive measures should be used, as there is no known antidote. It has been shown in a clinical trial that cholestyramine accelerates the elimination of meloxicam.

Shelf-Life:
3 years.

Storage Condition(s):
Store at temperature below 30°C

Product Description & Packing(s):
A round light yellow snap tablet, one side impressed with score in the middle, 'YSP' on the top and '15' on the bottom. " YSP 15 "

Blister packing of 10's x 3, 10's x 10, 10's x 50 & 10's x 100.

Y. S. P.®

Manufacturer and Product Registration Holder:
Y.S.P. INDUSTRIES (M) SDN. BHD. (199001001034)
Lot 3, 5, 7 & 12, Jalan P/7, Section 13,
Kawasan Perindustrian Bandar Baru Bangi,
43000 Kajang, Selangor, Malaysia.
Ordering Line:1 800 88 3027
Product Info: 1 800 88 3679

xxxxxx printing code xxxxxx

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