SUMMARY OF PRODUCT CHARACTERISTICS

1. **Name of the finished pharmaceutical product:**

   Melocam Tablet 7.5mg

2. **Qualitative and quantitative composition:**

   2.1 Qualitative Declaration:

   Meloxicam contains not less than 99.0% and not more than 101.0% of $C_{14}H_{13}N_3O_4S_2$, on dried substance.

   2.2 Quantitative Declaration:

   Each tablet contains:

   Meloxicam.....7.5mg

3. **Pharmaceutical form:**

   Tablet

4. **Clinical Particulars:**

   4.1 Therapeutic indication:

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

   4.2 Posology and method of administration:

   Osteoarthritis: 7.5mg daily, may be increased if necessary up to a maximum of 15mg daily.

   Rheumatoid Arthritis: 15mg daily. The dose may be reduced to 7.5mg daily according 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 daily.

The total daily dosage should not exceed 15mg.

The tablets should be taken with water or other fluid in conjunction with food.

4.3 Contraindication:

Meloxicam should not be given to patients who have developed signs of asthma, nasal polyps, angioedema or urticaria following the administration of acetylsalicylic acid and other NSAIDs. Meloxicam is contraindicated for patients with active ulceration, severe hepatic insufficiency and non-dialysed severe renal insufficiency.

Meloxicam should not be given to patients with hypersensitivity to NSAIDs, children and adolescents < 15 years, during pregnancy and breastfeeding.

4.4 Special warnings and special precautions for use:

Caution should be exercised in patients with a history of gastrointestinal disease and in patients receiving treatment with anticoagulants. Meloxicam should be withdrawn if peptic ulceration or gastrointestinal bleeding occurs. The consequences of such events are generally more serious in the elderly.

In patients with decreased renal blood flow and blood volume, administration of an NSAID may precipitate overt renal decompensation which is typically followed by recovery to pre-treatment state upon discontinuation of non-steroidal anti-inflammatory therapy. Dehydrated patients, those with congestive heart failure, liver cirrhosis, nephrotic syndrome and overt renal disease, those receiving a diuretic or those having undergone major surgical procedures which led to hypovolaemia are at greatest risk of such a reaction.

Meloxicam should be stopped and follow-up tests carried out if the abnormality elevations of serum transaminases or other parameters of liver function are significant or persistent.

Caution should be exercised in the treatment of the elderly who are more likely to be suffering from impaired renal, hepatic or cardiac function.

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 NSAIDs even in the 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 reports for fatal GI events.

4.5 Interaction with other FPPs and other forms of interaction:

a) Concomitant administration of more than one NSAID may increase the risk of gastrointestinal ulceration and bleeding through synergistic action.
b) Oral anticoagulants, ticlopidine, systemically administered heparin, thrombolytics: Increased risk of bleeding. Close monitoring of the effects of anticoagulants is required.
c) Lithium: Increased lithium plasma levels. It is recommended that plasma lithium levels be monitored when initiating, adjusting and discontinuing meloxicam.
d) Methotrexate: Meloxicam may increase the hematologic toxicity of methotrexate. Strict monitoring of blood cell count is recommended.
e) Contraception: Decrease the efficacy of intrauterine devices.
f) Diuretics: Patients receiving meloxicam and diuretics should be adequately hydrated and be monitored for renal function prior initiating treatment.

g) 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.

h) Cholestyramine binds meloxicam in the gastrointestinal tract leading to a faster elimination of Meloxicam.

i) Cyclosporin: Nephrotoxicity may be enhanced by NSAIDs via renal prostaglandin-mediated effects. Renal function is to be measured during combined treatment.

j) 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.

4.6 Pregnancy and lactation:

Meloxicam should not be used during pregnant and breast-feeding.

4.7 Effects on ability to drive and use machines:

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.

4.8 Undesirable effects:

a) 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.

b) Hematological: > 1%: Anemia; 0.1-1%: Disturbances of blood count, including differential white cell count, leukopenia and thrombocytopenia. Concomitant

administration of a potentially myelotoxic drug in particular methotrexate, appears to be a predisposing factor to the onset of cytopenia.

c) 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.
d) Respiratory: < 0.1%: Onset of acute asthma has been reported in certain individuals following NSAIDs including Meloxicam.
e) Central Nervous System: > 1%: lightheadedness and headache; 0.1-1%: Vertigo, tinnitus and drowsiness; < 0.1%: Confusion and disorientation.
f) Cardiovascular: > 1%: Oedema; 0.1-1%: Increase of blood pressure, palpitations and flushes.
g) Genitourinary: 0.1-1%: Abnormal renal function parameters (increased serum creatinine and/or serum urea); < 0.1%: Acute renal failure.
h) Vision Disorders: < 0.1%: Conjunctivitis, visual disturbances including blurred vision.
i) Hypersensitivity Reactions: < 0.1%: Angio-oedema and immediate hypersensitivity reactions including anaphylactoid / anaphylactic reactions.

4.9 Overdose:

The standard measures of gastric evacuation and general supportive measures should be used, as there is no known antidote. It has been shown in clinical trial that cholestyramine accelerates the elimination of meloxicam.

5. Pharmacological properties:

5.1 Pharmacodynamic properties:

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.

5.2 Pharmacokinetic properties:

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 0.4 – 1 µg/mL for 7.5mg 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, mild or moderate renal insufficiency do 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.

5.3 Preclinical safety data:

No information available.

6. Pharmaceutical particulars:

6.1 List of excipients:

(a) Microcrystalline Cellulose
(b) Povidone
(c) Colloidal Silicon Dioxide
(d) Sodium Starch Glycolate
(e) Lactose Monohydrate
(f) Magnesium Stearate
(g) Sodium Citrate

6.2 Incompatibilities:

No information available.

6.3 Shelf life:

2 years from the date of manufacture.

6.4 Special precautions for storage:

Store at temperature below 30°C. Protect from light and moisture.

6.5 Nature and contents of container:

Blister pack of 10's x10

6.6 Instructions for use and handling <and disposal>:

None has been mentioned.

7. Marketing authorization holder:

Name : Y. S. P. INDUSTRIES (M) SDN. BHD.

Address : Lot 3, 5 & 7, Jalan P/7, Section 13,
Kawasan Perindustrian Bandar Baru Bangi,
43000 Kajang, Selangor Darul Ehsan,
Malaysia.

8. Number(s) in the national register of finished pharmaceutical products:

06722/08064/REN/2021

9. **Date of first authorization / ~~renewal of the authorization~~:**
Oct 25, 2021

10. Date of revision of the text:

05 Aug 2020