SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MEFSAL 7.5 mg tablets
MEFSAL 15 mg, scored tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

MEFSAL 7.5 mg tablets:
Each tablet contains: 7.5 mg Meloxicam

MEFSAL 15 mg scored tablets:
Each tablet contains: 15 mg Meloxicam

Excipients with known effect: Lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

MEFSAL 7.5 mg tablet, in packs of 10 and 20, blister packed in PVC / PVDC / ALU
MEFSAL 15 mg scored tablet, in packs of 10 and 20, blister packed in PVC / PVDC / ALU

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Short-term symptomatic treatment of exacerbations of osteoarthritis.
- Long-term symptomatic treatment of rheumatoid arthritis
- Long-term symptomatic treatment of ankylosing spondylitis.

4.2 Posology and method of administration

Oral use
The total daily amount should be taken as a single dose, with water or another liquid, during a meal.
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).
The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically, especially in patients with osteoarthritis.

Exacerbations of osteoarthrosis:
7.5 mg/day (one tablet of 7.5 mg or half a tablet of 15 mg). If necessary, in the absence ofimprovement, the dose may be increased to 15 mg/day (two tablets of 7.5 mg, or one tablet of 15 mg).

Rheumatoid arthritis, ankylosing spondylitis:
15 mg / day (two 7.5 mg tablets or one 15 mg tablet)(see also section 'Special populations' below). According to the therapeutic response, the dose may be reduced to 7.5 mg/day (one 7.5 mg tablet or half a 15 mg tablet).
DO NOT EXCEED THE DOSE OF 15 MG/DAY.

Special populations
Elderly patients and patients with increased risks for adverse reaction (see section 5.2):
The recommended dose for long term treatment of rheumatoid arthritis and ankylosing spondylitis in elderly patients is 7.5 mg per day. Patients with increased risks for adverse reactions should start treatment with 7.5 mg per day (see section 4.4).

Renal impairment (see section 5.2):
In dialysis patients with severe renal failure, the dose should not exceed 7.5 mg 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 25 ml/min). (For patients with non-dialysed severe renal failure, see section 4.3)

Hepatic impairment (see section 5.2):
No dose reduction is required in patients with mild to moderate hepatic impairment (For patients with severely impaired liver function, see section 4.3)

Children and adolescents:
Meloxicam 7.5 mg tablets is contraindicated in children and adolescents aged under 16 years (see section 4.3).

4.3 Contraindications

This medicinal product is contra-indicated in the following situations:
- third trimester of pregnancy (see section 4.6 ‘Fertility, pregnancy and lactation’);
- children and adolescents aged under 16 years;
- hypersensitivity to meloxicam or to any of the excipients listed in section 6.1 or hypersensitivity to substances with a similar action, e.g. NSAIDs, aspirin. Meloxicam should not be given to patients who have developed signs of asthma, nasal polyps, angioneurotic 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)
- gastrointestinal bleeding, history of cerebrovascular bleeding or other bleeding disorders;

- severely impaired liver function;
- non-dialysed severe renal failure;
- severe heart failure.

4.4 Special warnings and precautions for use

- Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2 and paragraphs "Gastrointestinal Effects" and "Cardiovascular and Cerebrovascular Effects" below).
- The recommended maximum daily dose should not be exceeded in case of insufficient therapeutic effect, nor should an additional NSAID be added to the therapy because this may increase the toxicity while therapeutic advantage has not been proven.
  The use of Meloxicam with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.
  The use of Meloxicam is not appropriate for the treatment of acute pain.
  In the absence of improvement after several days, the benefit of the treatment should be reassessed.
- Any history of oesophagitis, gastritis and/or peptic ulcer must be sought in order to ensure their total cure before starting treatment with Meloxicam. Attention should routinely be paid to the possible onset of a recurrence in patients treated with Meloxicam and with a past history of this type.

Gastrointestinal effects

GI bleeding, ulceration or perforation which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events.

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 (see section 4.3), 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 (see below and 4.5)

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution is advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as heparin in curative or elderly patients, anticoagulants such as warfarin, other non steroidal anti-inflammatory drugs, including aspirin given at anti-inflammatory doses (≥ 1 g per dose or ≥3 g per day)(see section 4.5).

When GI bleeding or ulceration occurs in patients receiving Meloxicam the treatment should be withdrawn.

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section 4.8).

Cardiovascular and cerebrovascular effects

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedemahave been reported in association with NSAID therapy.

Clinical monitoring of blood pressure for patients at risk is recommended at baseline and especially during treatment initiation with Meloxicam.

Clinical trial and epidemiological data suggest that use of some NSAIDs including meloxicam (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). There are insufficient data to exclude such a risk for Meloxicam.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with Meloxicam after careful consideration.

Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes, or smoking).

Skin reactions:

Severe skin reactions, including fatal changes, including exfoliative dermatitis, Stevens-Johnson syndromes and Lyell syndromes, have been reported very rarely in NSAID treatments (see section 4.8).

The incidence of these undesirable effects appears to be greater at the beginning of treatment, with the onset of the disease occurring in the majority of cases during the first month of treatment. Treatment with Meloxicam should be discontinued as soon as skin rash, mucosal lesions or other signs of hypersensitivity develop.

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 uric acid and disorders of other biological parameters were observed. The majority of these instances involved transitory and slight abnormalities. Should any such abnormality prove significant or persistent, the administration of Meloxicam should be stopped and appropriate investigations undertaken.

Functional renal failure

NSAIDs, by inhibiting the vasodilating effect of renal prostaglandins, may induce a functional renal failure by reduction of glomerular filtration. This adverse event is dose-dependent. At the beginning of the treatment, or after dose increase, careful monitoring of diuresis and renal function is recommended in patients with the following risk factors:

- Elderly
- Concomitant treatments such as ACE (Angiotensin Converting Enzyme) inhibitors, angiotensin-II antagonists, sartans, diuretics (see section 4.5. Interaction with other medicinal products and other forms of interaction)

- Hypovolemia (whatever the cause)
- Congestive heart failure
- Renal failure
- Nephrotic syndrome
- Lupus nephropathy
- Severe hepatic dysfunction (serum albumin <25 g/l or Child-Pugh score ≥10)

In rare instance NSAIDs may be the cause of interstitial nephritis, glomerulonephritis, renal medullary necrosis or nephrotic syndrome.
The dose of meloxicam in patients with end-stage renal failure on haemodialysis should not be higher than 7.5 mg. 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:
Induction of sodium, potassium and water retention and interference with the natriuretic effects of diuretics may occur with NSAIDs. Furthermore, a decrease of the antihypertensive effect of antihypertensive drugs can occur (see section 4.5). Consequently, oedema, cardiac failure or hypertension may be precipitated or exacerbated in susceptible patients as a result. Clinical monitoring is therefore necessary for patients at risk. (see sections 4.2 and 4.3).

Hyperkalaemia
Hyperkalaemia can be favoured by diabetes or concomitant treatment with medicinal products known for their hyperkalaemic effect (see section 4.5.). Regular monitoring of potassium levels is recommended in these cases.

Other warnings and precautions
- Adverse reactions are often less well tolerated in elderly, fragile or weakened individuals, who therefore require careful monitoring. As with other NSAIDs, particular caution is required in the elderly, in whom renal, hepatic and cardiac functions are frequently impaired.
- The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2).
- Meloxicam, as any other NSAID may mask symptoms of an underlying infectious disease.
- The use of Meloxicam, as with any drug known to inhibit cyclooxygenase / prostaglandin synthesis, may impair fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving,or in which investigations of reproductive function are ongoing, discontinuation of Meloxicam therapy should be considered.
- Meloxicam tabletcontains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp-lactase deficiency of glucose galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults.

Pharmacodynamic Interactions:

- *Other non-steroidal anti-inflammatory drugs (NSAIDs) and aspirin > 3g/d:*

The concomitant administration of Meloxicam with other NSAIDS, including aspirin given at anti-inflammatory doses (≥1 g as single intake or ≥ 3 g per day) is not recommended (see section 4.4).

- *Corticosteroids (e.g. Glucocorticoids):*

The concomitant use with corticosteroids requests caution because of an increased risk of bleeding or gastrointestinal ulceration

- *Anticoagulant or heparin administered in geriatrics or at curative doses:*

Considerably increased risk of bleeding, via inhibition of platelet function and damage to the gastroduodenal mucosa.

NSAIDs may enhance the effects of anti-coagulants, such as warfarin (see section 4.4).

The concomitant use of NSAIDs and anti-coagulants or heparin administered in elderly or curative patients is not recommended (see section 4.4).

In remaining cases of heparin use caution is necessary due to an increased bleeding risk.

Careful monitoring of the INR is necessary if association can not be avoided.

- *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 (see section 4.4)

- *Diuretics, ACE inhibitors and Angiotensin-II Antagonists:*

NSAIDs may reduce the effect of diuretics and other antihypertensive drugs. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients) the co-administratin of an ACE inhibitor or Angiotensin-II antagonists and agents that inhibit cyclooxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the 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 at regular intervals (see section 4.4).

- *Other antihypertensive drugs (e.g. Beta-blockers):*

As in the case of ACE inhibitors and angiotensin II receptor antagonists, a decrease in the antihypertensive effect of beta-blockers may occur (due to inhibition of prostaglandins with vasodilatory effect).

- *Calcineurin inhibitors (e.g. cyclosporine, tacrolimus):*

Nephrotoxicity of calcineurin inhibitors may be enhanced by NSAIDs via renal prostaglandin mediated effects. During combined treatment renal function should be monitored, especially in the elderly.

- *Intrauterine devices:*

NSAIDs have been reported to decrease the efficacy of intrauterine devices.

However, this reduction in the efficacy of intrauterine devices previously reported for NSAID treatments needs to be confirmed.

Pharmacokinetic interactions (effect of Meloxicam on the pharmacokinetics of other drugs):

- ***Lithium:***

NSAIDs have been reported to increase blood lithium levels via decreased renal excretion of lithium, which may reach toxic values. The concomitant use of lithium and NSAIDs is not recommended (see section 4.4). If this combination appears necessary, lithium 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 15 mg/week) the concomitant use of NSAIDs is not recommended (see section 4.4).

The risk of an interaction between NSAID preparations and methotrexate, should be considered also in patients on low dosage of methotrexate, especially in patients with impaired renal function.

In case combination treatment is necessary, blood cell count and the renal function should be monitored. 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.

Although the pharmacokinetics of methotrexate (15mg/week) were not relevantly affected by concomitant Meloxicam treatment, it should be considered that the haematological toxicity of methotrexate can be amplified by treatment with NSAID drugs (see above). (See section 4.8)

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. This interaction is of clinical significance.

No direct pharmacokinetic interaction with clinical relevance was detected with antacids, cimetidine or digoxin.

4.6 Pregnancy and breast feeding:

- ***Pregnancy***

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin

synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5 %. The risk is believed to increase with dose and duration of therapy.
In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.
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.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose

- The foetus to:
  - cardiopulmonary toxicity (with premature closure of the ductusarteriosus and pulmonary hypertension);
  - renal dysfunction, which may progress to renal failure with oligo-hydroamniosis;
- The mother and the neonate, at the end of pregnancy, to:
  - Possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
  - Inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, Meloxicam is contraindicated during the third trimester of pregnancy.

- ***Breast feeding***

While no specific experience exists for Meloxicam, NSAIDs are known to pass into mother's milk. Administration therefore is not recommended in women who are breastfeeding.

4.7 Effects on ability to drive and use machines

No specific studies on the effect on the ability to drive and use machineries have been performed. However, on the basis of the pharmacodynamic profile and reported adverse drug reactions, 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

4.8 Undesirable effects

a) General Description

Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).
Oedema, 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 (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4 - Special warnings and precautions for use) have been reported following administration. Less frequently, gastritis has been observed.
The frequencies of adverse drug reactions given below are based on corresponding occurrences of reported adverse events in 27 clinical trials with a treatment duration of at least 14 days. The information is based on clinical trials involving 15197 patients who have been treated with daily oral doses of 7.5 or 15 mg of Meloxicam over a period of up to one year.
Adverse drug reactions that have come to light as a result of reports received in relation to administration of the marketed product are included
Adverse reactions have been ranked under headings of frequency using the following convention: Very common (≥ 1/10); common (≥ 1/100. < 1/10); uncommon (≥ 1/1.000, < 1/100); rare (≥ 1/10.000, < 1/1.000); very rare (< 1/10.000), not known (cannot be estimated from the available data).

b) Table of adverse reactions

Blood and the lymphatic system disorders
Uncommon: Anaemia
Rare: Disturbances of blood count (including differential white cell count), leucocytopenia ; thrombocytopenia
Very rare cases of agranulocytosis have been reported (see section c).

Immune system disorders
Uncommon: Allergic reactions other than anaphylactic or anaphylactoid reactions
Not known: Anaphylactic / anaphylactoid reactions

Psychiatric disorders
Rare :Mood disorders, nightmares
Not known: Confusional state, disorientation

Nervous system disorders
Common: Headache
Uncommon: Dizziness, somnolence

Eye disorders
Rare: Visual disturbances including blurred vision, 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 : Hypertension (see section 4.4), flushing

Respiratory, thoracic and mediastinal disorders
Rare: Asthma in individuals allergic to acetylsalicylic acid or other NSAIDs

Gastrointestinal disorders
Very common: Dyspepsia, nausea, vomiting, abdominal pain, constipation, flatulence, diarrhoea
Uncommon: Occult or macroscopic gastrointestinal haemorrhage, stomatitis, gastritis, eructation
Rare: Colitis, gastroduodenal ulcers, oesophagitis
Very rare:Gastrointestinal perforation
Gastrointestinal haemorrhage, ulceration or perforation may sometimes be severe and potentially fatal, especially in elderly (see section 4.4).

Hepatobiliary disorders
Uncommon: Liver function test disorder (e.g. raised transaminases or bilirubin),
Veryrare: Hepatitis

Skin and subcutaneous tissue disorders
Uncommon: Angioedema, pruritus, rash
Rare:): Stevens-Johnson syndrome, Lyell syndrome, urticaria
Veryrare: Dermatitisbullous, erythema multiforme
Not known: Photosensitivity reactions

Renal and urinary disorders
Uncommon: Sodium and water retention, hyperkalaemia (see sections 4.4. and 4.5.), renal function test abnormal (increased serum creatinine and/or serum urea)
Very rare: Acute renal failure in particular in patients with risk factors (see section 4.4.)

General disorders and administration site conditions
Uncommon: Oedema including oedema of the lower limbs.

c) Information Characterising Individual Serious or Frequently Occurring Adverse Reactions

Very rare cases of agranulocytos is have been reported in patients treated with Meloxicam and other potentially myelotoxic drugs (see section 4.5).

d) Adverse reactions which have not been observed yet in relation to the product, but which are generallyaccepted as being attributable to other compounds in the class

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 (see section 4.4).

4.9 Overdose

Symptoms following acute NSAID overdose are usually limited to lethargy, drowsiness, nausea, vomiting and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur.Severe poisoning may result in hypertension, acute renal failure, hepatic dysfunction, respiratory depression, coma, convulsions, cardiovascular collapse and cardiac arrest. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs and may occur following an overdose.

In case of overdose with NSAIDs, appropriate symptomatic treatment should be initiated.

Accelerated removal of Meloxicam by 4 g oral doses of cholestyramine given three times a day was demonstrated in a clinical trial.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Non Steroidal Anti-Inflammatory agent, Oxicams

ATC Code: M01AC06

Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam family, with anti-inflammatory, analgesic and antipyretic properties.

The anti-inflammatory activity of Meloxicam has been proven in classical models of inflammation. As withother NSAIDs, its precise mechanism of action remains unknown. However, there is at least one common mode of action shared by all NSAIDs (including Meloxicam): inhibition of the biosynthesis of prostaglandins, known inflammation mediators

5.2 Pharmacokinetic properties

Absorption

Meloxicam is well absorbed from the gastrointestinal tract, which is reflected by a high absolutebioavailability of 89% following oral administration (capsule).

Following single dose administration of Meloxicam, mean maximum plasma concentrations are achievedwithin 5-6 hours with solid oral dosage forms (tablets).

With multiple dosing, steady state conditions were reached within 3 to 5 days. Once daily dosing leads todrug plasma concentrations with a relatively small peak-trough fluctuation in the range of 0.4 - 1.0 µg/mL for 7.5 mg doses and 0.8 - 2.0 µg/mL for 15 mg doses, respectively (C_{min} and C_{max} at steady state, respectively). Maximum plasma concentrations of Meloxicam at steady state, are achieved within 5 to 6 hours for the tablet. Continuous treatment for periods of more than one year results in similar drug concentrations to those seen once steady state is first achieved. The absorption of Meloxicam after oral administration is not altered when administered in the middle of a meal.

Distribution

Meloxicam is very strongly bound to plasma proteins, essentially albumin (99%). Meloxicam penetrates intosynovial fluid to give concentrations approximately half of those in plasma. Volume of distribution is low, on average 11 L. Inter individual variation is the order of 30-40%.

Biotransformation

Meloxicam undergoes extensive hepatic biotransformation. Four different metabolites of Meloxicamwere 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). In vitro studies suggest that CYP 2C9 plays an important role in this metabolic pathway, with a minor contribution from the CYP 3A4 isoenzyme. The patient's peroxidase activity is probably responsible for the other two metabolites, which account for 16% and 4% of the administered dose respectively.

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. The mean elimination half-life is about 20 hours. Total plasma clearance amounts on average 8 mL/min.

Linearity/non-linearity

Meloxicam demonstrates linear pharmacokinetics in the therapeutic dose range of 7.5 mg 15 mg following per oral administration.

Special populations

Hepatic/renal Insufficiency:

Neither hepatic, mild nor moderate renal insufficiency have a substantial effect on Meloxicam pharmacokinetics. In terminal renal failure, the increase in the volume of distribution may result in higher free Meloxicam concentrations, and a daily dose of 7.5 mg must not be exceeded (see section 4.2).

Elderly:

Mean plasma clearance at steady state in elderly subjects was slightly lower than that reported for younger subjects.

5.3 Preclinical safety data

The toxicological profile of Meloxicam has been found in preclinical studies to be identical to that ofNSAIDs: gastrointestinal ulcers and erosions, renal papillary necrosis at high doses during chronicadministration in two animal species.

Oral reproductive studies in the rat have shown a decrease of ovulations and inhibition of implantations andembryotoxic effects (increase of resorptions) at maternotoxic dose levels at 1mg/kg and higher. Studies of toxicity on reproduction in rats and rabbits did not reveal teratogenicity up to oral doses of 4 mg/kg in rats and 80 mg/kg in rabbits.
The affected dose levels exceeded the clinical dose (7.5-15 mg) by a factor of 10 to 5-fold on a mg/kg dosebasis (75 kg person). Foetotoxic effects at the end of gestation, shared by all prostaglandin synthesisinhibitors, have been described. No evidence has been found of any mutagenic effect, either in vitro or in vivo. No carcinogenic risk has been found in the rat and mouse at doses far higher than those used clinically.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Pregelatinised Maize Starch
Lactose monohydrate
Maize starch
Sodium citrate
Microcrystalline cellulose
Colloidal anhydrous silica
Magnesium stearate

6.2 Incompatibilities
Not applicable

6.3 Shelf life
36 months

6.4 Special precautions for storage
This medicinal product is stored in its original packaging, sheltered from humidity

6.5 Nature and contents of container
PVC/PVDC/Aluminium blister, packs of 10 and 20 tablets.

6.6 Special precautions for disposal
No special requirements

7. MARKETING AUTHORISATION HOLDER
COOPER PHARMA
41, Rue Mohamed DIOURI,
20 110 Casablanca, Morocco.

8. MARKETING AUTHORISATION NUMBER
Mefsal 7,5 mg pack of 10: 247/16DMP/21/NRQ
Mefsal 7,5 mg pack of 20: 248/16DMP/21/NRQ

Mefsal 15 mg pack of 10: 249/16DMP/21/NRQ
Mefsal 15 mg pack of 20: 250/16DMP/21/NRQ

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Mefsal 7,5 mg & 15 mg pack of 10
Date of first authorisation: 18/05/2011
Date of last renewal: 25/05/2016
Mefsal 7,5 mg & 15 mg pack of 20
Date of first authorisation: 02/09/2010
Date of last renewal: 25/05/2016

10. DATE OF REVISION OF THE TEXT

XX/XX/XXXX

Legal categories
POM - Prescription Only Medicine