

FLEXOCAM 7,5 mg

FLEXOCAM 15 mg

SCHEDULING STATUS:

S3

PROPRIETARY NAME AND DOSAGE FORM:

FLEXOCAM 7,5 mg tablets

FLEXOCAM 15 mg tablets

COMPOSITION:

Each **FLEXOCAM 7,5 mg** tablet contains 7,5 mg meloxicam.

Each **FLEXOCAM 15 mg** tablet contains 15 mg meloxicam.

PHARMACOLOGICAL CLASSIFICATION:

A 3.1 Antirheumatics (anti-inflammatory agents)

PHARMACOLOGICAL ACTION:

Meloxicam, an oxicam (enolic acid) derivative, is a non-steroidal anti-inflammatory compound (NSAID) with analgesic, antipyretic and anti-inflammatory activities. The action of meloxicam is related to inhibition of the enzyme cyclo-oxygenase (COX), resulting in the decreased formation of prostaglandins (mediators of inflammation) and thromboxanes. A selective COX-2 inhibitory (anti-inflammatory effect) *in vitro* in relation

to COX-1 has been demonstrated. Inhibition of COX-1 (gastrointestinal, renal and platelet effects) *in vivo* occurs. It is suggested that the extent of inhibition of COX-1 *in vivo* is a function of dose and inter-individual variability of meloxicam concentrations.

Pharmacokinetics:

The extent of absorption after oral administration is 89% and concomitant administration with food does not affect absorption. Meloxicam is 99% protein bound and has an elimination half-life of 15-20 hours. Meloxicam is extensively metabolised in the liver (mainly by oxidation) and less than 5% of the daily dose is excreted unchanged in the faeces and urine.

INDICATIONS:

FLEXOCAM is indicated for the symptomatic treatment of:

- Rheumatoid arthritis
- Painful osteoarthritis
- Ankylosing spondylitis
- Episodes of acute sciatica

CONTRA-INDICATIONS:

- Hypersensitivity to **FLEXOCAM** or to any components of the formulation.
- Patients in whom attacks of asthma, urticaria, nasal polyps or acute rhinitis are precipitated by acetylsalicylic acid/ aspirin or by other non-steroidal anti-inflammatory agents.

- Active peptic ulcer disease.
- Severe hepatic impairment.
- Severe non dialysed renal impairment.
- Pregnancy. (see PREGNANCY AND LACTATION)

WARNINGS:

- Children under the age of 18 years- Safety and efficacy have not been established.
- **FLEXOCAM** should be used with caution in patients with: -
- Gastrointestinal bleeding.
- Hepatic impairment – Increases risk of renal decompensation.
- Renal impairment – Increases risk of renal decompensation.
- Congestive heart failure – Increase risk of renal decompensation.

INTERACTIONS:

- **Acetylsalicylic acid/ Aspirin and other NSAIDS** – May result in an increase in gastric ulceration and/or bleeding.
- **Warfarin and other anticoagulants** – Increase the risk of bleeding complications.
- **Lithium** – May result in an increase in plasma lithium concentrations. Monitor lithium plasma concentrations carefully when therapy with **FLEXOCAM** is initiated or withdrawn.

- **Methotrexate** – May result in increased haematological toxicity due to methotrexate toxicity.
- **Angiotensin-converting enzyme (ACE) inhibitors and other anti-hypersensitivity agents** – May result in a decrease in antihypertensive effects and an increased risk of renal failure.
- **Cholestyramine** - May result in a reduced therapeutic effect of **FLEXOCAM**.
- **Ciclosporin** – Increases the risk of nephrotoxicity.
- **Alcohol** - Simultaneous intake may increase the risk of bleeding.
- **Diuretics** – May result in renal impairment if the patient is dehydrated (see Precautions).
- **Intrauterine device** – NSAIDS may decrease the efficacy of intrauterine devices.

PREGNANCY AND LACTATION:

Safety and efficacy in pregnancy and lactation has not been established. The use of **FLEXOCAM** during the third trimester is not recommended because of possible adverse effects on the foetus, such as premature closure of the ductus arteriosus, which may lead to persistent pulmonary hypertension in the newborn. See CONTRA-INDICATIONS.

DOSAGE AND DIRECTIONS FOR USE:

Safety and efficacy in children under the age of 18 years has not been established. The tablet should be taken with a glass of water and together with a meal.

The dose of **FLEXOCAM** in patients with end stage renal disease on haemodialysis should not be greater than 7,5 mg/day. (No dosage reduction is necessary in patients with mild to moderate renal impairment).

Adults:

The maximum daily dose of **FLEXOCAM** is 15 mg.

Acute sciatica: 7,5 mg once daily. If there is no improvement the dose can be increased to 15 mg a day.

Ankylosing spondylitis: 15 mg once daily

Osteoarthritis: 7,5 mg once daily. Increase to 15 mg if necessary.

Rheumatoid arthritis: 15 mg once daily. Reduce dose if possible (provided therapeutic response is maintained).

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side effects:

Haematological:

- *Frequent:* Anaemia
- *Less frequent:* Thrombocytopenia, neutropenia, eosinophilia, agranulocytosis, leukopenia

Cardiovascular:

- *Frequent:* Oedema
- *Less frequent:* Palpitations, elevated blood pressure

Neurological:

- *Frequent:* Headache, dizziness, light-headedness
- *Less frequent:* Vertigo, confusion, drowsiness, insomnia, nightmares

Gastrointestinal:

- *Frequent:* Dyspepsia, nausea and vomiting, diarrhoea, flatulence, constipation and abdominal pain
- *Less frequent:* Gastrointestinal bleeding, perforation or ulceration (generally more serious in the elderly), induction or exacerbation of colitis, gastritis

Kidney/Genitourinary:

- *Less frequent:* Nephrotic syndrome, glomerulonephritis, interstitial nephritis and papillary necrosis, renal failure

Liver:

- *Less frequent:* Hepatitis

Ocular:

- *Less frequent:* Visual disturbances (such as blurred vision), conjunctivitis

Respiratory:

- *Less frequent:* Bronchospasm (see other)

Skin:

- *Frequent:* Pruritus, rash
- *Less frequent:* Flushing, urticaria, stomatitis, photosensitivity, bullous dermatoses, including erythema multiforme and Stevens-Johnson syndrome, toxic epidermal necrolysis

Other:

- *Less frequent:* tinnitus, hypersensitivity reactions including anaphylaxis, angioedema and bronchospasm (especially if patient is aspirin-sensitive and has asthma and/or nasal polyps, **FLEXOCAM** should be withdrawn immediately)

Special Precautions:

Patients with a history of gastrointestinal disease should be monitored very carefully while on **FLEXOCAM** and therapy should be discontinued if any ulceration or bleeding occurs.

Patients should not operate machinery or drive a vehicle if they experience drowsiness, blurred vision or any other central nervous system effect.

Patients who are dehydrated, have heart failure, hepatic or renal dysfunction, taking diuretics or have undergone surgery leading to hypovolaemia, are at particular renal discompensation and renal function should be carefully monitored.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS

TREATMENT:

Symptoms of overdose:

(See SIDE EFFECTS AND SPECIAL PRECAUTIONS).

Treatment of overdose:

Treatment is symptomatic and supportive as there is no known antidote.

Absorption should be reduced by:

- Activated charcoal if patient presents 1 to 2 hours after overdose
- Cholestyramine
- Gastric lavage if within 1 hour of overdose.

IDENTIFICATION:

FLEXOCAM 7,5 tablets: Light yellow, round biconvex, bevelled edged tablet with B and 18 debossed on one side and plain on the reverse.

FLEXOCAM 15 tablets: Light yellow, round biconvex, bevelled edged tablet with B and 19 debossed on either side of breakline on one side and plain on the reverse.

PRESENTATION:

FLEXOCAM 7,5 tablets: Hard Aluminium/opaque PVC blister packs of 30 tablets (strips of 10's) in an outer carton.

FLEXOCAM 15 tablets: Hard Aluminium/opaque PVC blister packs of 10 tablets or 30 tablets (strips of 10's) in an outer carton

STORAGE INSTRUCTIONS:

Store below 25°C. Protect from light.

The blisters should not be removed from the carton until required for use.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBERS:

FLEXOCAM 7,5 mg tablets: 38/3.1/0497

FLEXOCAM 15 mg tablets: 38/3.1/0498

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Pharma Dynamics (Pty) Ltd

F02 Grapevine House

Steenberg Office Park

Westlake

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DATE OF PUBLICATION OF THE PACKAGE INSERT:

9 March 2005

FLEXOCAM 7,5 mg

FLEXOCAM 15 mg

SKEDULERINGSSTATUS:

S3

EIENDOMSNAAM EN DOSEERVORM:

FLEXOCAM 7,5 mg tablette

FLEXOCAM 15 mg tablette

SAMESTELLING:

Elke **FLEXOCAM 7,5 mg** tablet bevat 7,5 mg meloksikam.

Elke **FLEXOCAM 15 mg** tablet bevat 15 mg meloksikam.

FARMAKOLOGIESE KLASSIFIKASIE:

A.3.1 Anti-rumatiese middels (anti-inflammatoriese middels).

FARMAKOLOGIESE WERKING:

Meloksikam, 'n oksikam(enolsuur)-derivaat, is 'n nie-steroïedale anti-inflammatoriese middel (NSAIM) met pynstillende, koorswerende en anti-inflammatoriese aktiwiteite. Die werking van meloksikam is verwant aan inhibisie van die siklo-oksigenase (COX) ensiem, wat verminderde vorming van prostaglandiene (bemiddelaars van inflammasie) en tromboksane veroorsaak. 'n Selektiewe COX-2-inhibisie (anti-inflammatoriese

uitwerking) in verhouding tot COX-1 kon *in vitro* bewys word. Inhibisie van COX-1 (gastroïntestinale, renale en plaatjie-uitwerkings) vind *in vivo* plaas.

Dit word gesuggereer dat die mate van *in vivo* COX-1-inhibisie 'n funksie van dosis en inter-individuele variasie van meloksikamkonsentrasies is.

Farmakokinetika:

Die omvang van absorpsie na orale toediening is 89% en gelyktydige toediening saam met voedsel het geen invloed op absorpsie nie. Meloksikam is 99% proteïengebonde en het 'n eliminasië halfleeftyd van 15 - 20 uur. Meloksikam word ekstensief in die lewer gemetaboliseer (hoofsaaklik deur oksidasie) en minder as 5% van die daaglikse dosis word onveranderd in die faeces en urine uitgeskei.

INDIKASIES:

FLEXOCAM word aangedui vir die simptomatiesse behandeling van:

- Rumatoïede artritis
- Pynlike osteoartritis
- Ankiloserende spondilitis
- Episodes van akute iskias

KONTRA-INDIKASIES:

- Hipersensitiwiteit teenoor **FLEXOCAM** of enigeen van die bestanddele van die formulering.

- Pasiënte by wie asma-aanvalle, urtikarie, nasale poliepe of akute rinitis uitgelok word deur asetielsalisielsuur/aspirien of deur ander nie-steroïedale anti-inflammatoriese middels.
- Aktiewe peptiese ulkus.
- Ernstige hepatiese inkorting.
- Ernstige nie-gedialiseerde nierinkorting.
- Swangerskap (Sien SWANGERSKAP EN LAKTASIE).

WAARSKUWINGS:

- Kinders jonger as 18 jaar - Veiligheid en doeltreffendheid is nie vasgestel nie.
- **FLEXOCAM** moet met omsigtigheid gebruik word in pasiënte met:-
- Gastroïntestinale bloeding.
- Hepatiese inkorting - Verhoog die risiko van renale dekompensasie.
- Renale inkorting - Verhoog die risiko van renale dekompensasie.
- Kongestiewe hartversaking - Verhoog die risiko van renale dekompensasie.

INTERAKSIES:

- **Asetielsalisielsuur/aspirien en ander NSAIMS** - Mag 'n toename van gastriese ulserasie en/of bloeding veroorsaak.
- **Warfarien en ander antikoagulate** - Verhoog die risiko van bloedingskomplikasies.

- **Litium** - Mag 'n verhoging in plasmalitiumkonsentrasies veroorsaak. Moniteer plasmalitiumkonsentrasies versigtig wanneer terapie met **FLEXOCAM** begin en onttrek word.
- **Metotreksaat** - Mag verhoogde hematologiese toksisiteit as gevolg van metotreksaat-toksisiteit veroorsaak.
- **Angiotensien-omsettingsensiem(AOE)inhibeerders en ander antihipertensie middels** - Mag 'n verlaging in antihipertensie uitwerkings en 'n verhoogde risiko van nierversaking veroorsaak.
- **Cholestiramien** - Mag 'n verminderde terapeutiese uitwerking van **FLEXOCAM** veroorsaak.
- **Siklosporien** - Verhoog die risiko van nefrotoksisiteit.
- **Alkohol** - Gelyktydige inname mag die risiko van bloeding verhoog.
- **Diuretika** - Mag nierinkorting veroorsaak indien die pasiënt gedehidreer is (sien Voorsorgmaatreëls).
- **Intra-uteriene kontraseptiewe apparaat** - NSAIMS mag die doeltreffendheid van intra-uteriene apparate verminder.

SWANGERSKAP EN LAKTASIE:

Veiligheid en doeltreffendheid in swangerskap en laktasie is nie vasgestel nie. Die gebruik van **FLEXOCAM** tydens die derde trimester van swangerskap word nie aanbeveel nie as gevolg van moontlike nadelige uitwerkings op die fetus, soos premature sluiting van die ductus arteriosus, wat tot aanhoudende pulmonale hipertensie in die pasgeborene mag lei. Sien KONTRA-INDIKASIES.

DOSIS EN GEBRUIKSAANWYSINGS:

Veiligheid en doeltreffendheid in kinders jonger as 18 jaar is nie vasgestel nie.

Die tablet behoort met 'n glas water en saam met 'n maaltyd geneem te word.

Die dosis **FLEXOCAM** in pasiënte met endstadium renale siekte op hemodialise behoort 7,5 mg/dag nie te oorskry nie. (Geen dosisvermindering is in pasiënte met ligte tot matige nierinkorting noodsaaklik nie).

Volwassenes:

Die maksimum daaglikse dosis van **FLEXOCAM** is 15 mg.

Akute iskias: 7,5 mg een keer per dag. Indien geen verbetering intree nie, kan die dosis tot 15 mg per dag verhoog word.

Ankiloserende spondylitis: 15 mg een keer per dag.

Osteoartritis: 7,5 mg een keer per dag. Verhoog tot 15 mg indien nodig.

Rumatoïede artritis: 15 mg een keer per dag. Verminder dosis indien moontlik (mits terapeutiese reaksie bewaar word).

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS:

Newe-effekte:

Hematologies:

- *Frekwent:* Anemie.
- *Minder frekwent:* Trombositopenie, neutropenie, eosinofilie, agranulositose, leukopenie.

Kardiovaskulêr:

- *Frekwent*: Edeem.
- *Minder frekwent*: Hartkloppings, verhoogde bloeddruk.

Neurologies:

- *Frekwent*: Hoofpyn, duiseligheid, lighoofdigheid.
- *Minder frekwent*: Vertigo, verwarring, slaperigheid, slaaploosheid, nagmerries.

Gastroïntestinaal:

- *Frekwent*: Dispepsie, naarheid en braking, diarree, winde, hardlywigheid en abdominale pyn.
- *Minder frekwent*: Gastroïntestinale bloeding, perforasie of ulserasie (gewoonlik ernstiger in bejaardes), induksie of verergering van kolitis, gastritis.

Nier/ Genito-urinêr:

- *Minder frekwent*: Nefrotiese sindroom, glomerulonefritis, interstisiële nefritis, papillêre nekrose, nierversaking.

Lewer:

- *Minder frekwent*: Hepatitis.

Okulêr:

- *Minder frekwent*: Versteurings van visie (soos versteurde visie), konjunktivitis.

Respiratories:

- *Minder frekwent*: Brongospasma (sien Ander).

Vel:

- *Frekwent*: Pruritus, veluitslag.

- *Minder frekwent:* Blossing, urtikarie, stomatitis, fotosensitiwiteit, bulleuse dermatoses, insluitend erythema multiforme en Stevens-Johnson-sindroom, toksiese epidermale nekrolise.

Ander:

- *Minder frekwent:* Tinnitus, hipersensitiwiteitsreaksies insluitend anafilakse, angio-edeem en brongospasma (veral as die pasiënt aspirien-sensitief is en aan asma en/of nasale poliepe ly, FLEXOCAM moet onmiddellik onttrek word).

Spesiale Voorsorgmaatreëls:

Pasiënte met 'n geskiedenis van gastroïntestinale siekte moet baie versigtig gemonitor word terwyl hulle op **FLEXOCAM** is en terapie moet gestaak word indien enige ulserasie of bloeding voorkom.

Pasiënte moet nie masjiene hanteer of 'n voertuig bestuur indien hulle slaperigheid, versteurde visie of enige ander sentrale sensusisteem effek ondervind nie.

Pasiënte wat gedehidreer is, aan hartversaking, hepatiese of renale disfunksie ly, diuretika neem of chirurgie ondergaan het wat tot hipovolemie lei, is aan besondere risiko van renale dekompensasie blootgestel en nierfunksie moet versigtig gemoniteer word.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE

BEHANDELING DAARVAN:

Simptome van oordosering:

(Sien NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS).

Behandeling van oordosering:

Behandeling is simptome en ondersteunend omdat geen teenmiddel bekend is nie.

Absorpsie moet deur die volgende verminder word:

- Geaktiveerde houtskool indien die pasiënt 1 tot 2 uur na oordosis presenteer
- Cholestiramien
- Maagspoeling indien 1 uur na oordosis.

IDENTIFIKASIE:

FLEXOCAM 7,5 mg tablette: Liggeel, ronde bikonvekse tablette met afgeplatte kante, B en 18 gebosseleer op een kant en onversier op die agterkant.

FLEXOCAM 15 mg tablette: Liggeel, ronde bikonvekse tablette met afgeplatte kante, B en 19 gebosseleer op weerskante van die keep op een kant en onversier op die agterkant.

AANBIEDING:

FLEXOCAM 7,5 tablette: Harde aluminium/opake PVC stulpverpakkings van 30 tablette (in stroke van 10) in 'n buitenste karton.

FLEXOCAM 15 tablette: Harde aluminium/opake PVC stulpverpakkings van

10 tablette of 30 tablette (in stroke van 10) in 'n buitenste
karton.

BERGINGSAAWYSINGS:

Bewaar benede 25°C. Beskerm teen lig.

Moenie die stulpverpakkings uit die karton verwyder totdat dit benodig word nie.

HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS:

FLEXOCAM 7,5 mg tablette: 38/3.1/0497

FLEXOCAM 15 mg tablette: 38/3.1/0498

NAAM EN BESIGHEIDSADRES VAN HOUER VAN DIE SERTIFIKAAT VAN

REGISTRASIE:

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DATUM VAN PUBLIKASIE VAN DIE VOUBILJET:

9 Maart 2005