Spedicam®
(Lornoxicam 8 mg)

اسپیڈی کیم

COMPOSITION

SPEDICAM 8 mg Tablet
Each film coated tablet contains:
Lornoxicam…….. 8 mg
(Pharmevo Specs.)

DESCRIPTION

SPEDICAM (Lornoxicam) is a non-steroidal anti-inflammatory drug with analgesic properties and belongs to the class of oxicams. It is chemically designated as (3E)-6-chloro-3-[hydroxy(pyridin-2-ylamino)methylene]-2-methyl-2,3-dihydro-4H-thieno[2,3-e][1,2]thiazin-4-one 1,1-dioxide. The molecular formula of Lornoxicam is $C_{13}H_{10}ClN_3O_4S_2$

CLINICAL PHARMACOLOGY

Mechanism of Action
Lornoxicam is a non-steroidal anti-inflammatory drug with analgesic properties and belongs to the class of oxicams. Lornoxicam's mode of action is mainly related to the inhibition of the prostaglandin synthesis (inhibition of the cyclooxygenase enzyme) leading to de-sensitisation of peripheral nociceptors and consequently inhibition of inflammation. A central effect on nociception which seems to be independent of anti-inflammatory effects has also been suggested.
Lornoxicam has no effect on vital signs (e.g. body temperature, respiratory rate, heart rate, blood pressure, ECG, spirometry).
The analgesic properties of Lornoxicam have been demonstrated successfully in several clinical trials during development of the drug.
Due to a local gastrointestinal irritation and a systemic ulcerogenic effect related to the inhibition of prostaglandin (PG)-synthesis, gastrointestinal sequela are common undesirable effects after treatment with Lornoxicam as seen with other NSAIDs.

Pharmacokinetics

Absorption
Lornoxicam is absorbed rapidly and almost completely from the gastrointestinal tract. Maximum plasma concentrations are achieved after approximately 1-2 hours. The absolute bioavailability of lornoxicam is 90-100 %. No first-pass effect has been observed. The mean elimination half-life is 3-4 hours.
Simultaneous intake of Lornoxicam with meals reduces Cmax by approximately 30 % and Tmax increases from 1.5 to 2.3 hours. The absorption of Lornoxicam (calculated on AUC) can be reduced up to 20 %.

Distribution
Lornoxicam is found in the plasma in unchanged form and as its hydroxylated metabolite. The plasma protein binding of Lornoxicam is 99 % and not concentration dependent.

Metabolism
Lornoxicam is extensively metabolized in the liver, primarily to the inactive 5–hydroxy-lornoxicam by hydroxylation. CYP2C9 is involved in this biotransformation of lornoxicam. Due to genetic polymorphism, slow and extensive metabolizers exist for this enzyme which could result in markedly increased plasma levels of Lornoxicam in slow metabolizers. The hydroxylated metabolite exhibits no pharmacological activity. Lornoxicam is metabolized completely, and approximately 2/3rd is eliminated via the liver and 1/3rd via the kidneys as inactive substance.

Excretion
The mean elimination half-life of the parent compound is 3 to 4 hours. After oral administration about 50% is excreted in the feces and 42% through the kidneys, mainly as 5-hydroxylornoxicam. The elimination half-life of 5-hydroxylornoxicam is about 9 hours after a parenteral single or twice daily dose.
In elderly patients above age 65, the clearance is reduced with 30-40%. Apart from reduced clearance, there is no significant change in the kinetic profile of Lornoxicam in elderly patients.
There is no significant change in the kinetic profile of Lornoxicam in patients with renal or hepatic failure, except for accumulation in patients with chronic liver disease after 7 days of treatment with daily doses of 12 and 16 mg.

INDICATIONS

SPEDICAM is indicated in:
- Short-term relief of acute mild to moderate pain
- Symptomatic relief of pain and inflammation in osteoarthritis
- Symptomatic relief of pain and inflammation in rheumatoid arthritis

DOSAGE AND ADMINISTRATION

For all patients the appropriate dosing regimen should be based upon individual response to treatment.

Pain
Dose of 8-16 mg Lornoxicam daily divided into 2 or 3 doses. Maximum recommended daily dose is 16 mg.

Osteoarthritis and Rheumatoid arthritis
Initial recommended dose is 12 mg Lornoxicam daily divided into 2 or 3 doses. Maintenance dose should not exceed 16 mg Lornoxicam daily.

Dosing considerations in special populations

Renal impairment
For patients with mild to moderate renal impairment the maximum recommended daily dose is 12 mg divided in 2 or 3 doses

Hepatic impairment
For patients with moderate hepatic impairment the maximum recommended daily dose is 12 mg divided in 2 or 3 doses.

Administration requirements
SPEDICAM tablets are for oral use and should be taken with a sufficient quantity of liquid.

CONTRAINDICATIONS

- Hypersensitivity to Lornoxicam
- Thrombocytopenia
- Hypersensitivity (symptoms like asthma, rhinitis, angioedema or urticaria) to other NSAIDs including acetylsalicylic acid
- Severe heart failure.
- Gastro-intestinal bleeding, cerebrovascular bleeding or other bleeding disorders
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy
- Active or history of recurrent peptic ulcer/hemorrhage (two or more distinct episodes of proven ulceration or bleeding)
- Severe hepatic impairment
- Severe renal impairment
- The third trimester of pregnancy

WARNINGS AND PRECAUTIONS

Renal impairment
Lornoxicam should be administered with precaution in patients with mild to moderate renal impairment due to dependency on renal prostaglandins for maintenance of renal blood flow. Treatment with Lornoxicam should be discontinued if renal function deteriorates during treatment.
Renal functions should be monitored in patients who undergo major surgery, with cardiac failure, receiving treatment with diuretics, receiving concomitant treatment with drugs that are suspected to or known to be able to cause kidney damage.

Patients with blood coagulation disorders
Lornoxicam reduces platelet aggregation and prolongs bleeding time and consequently care should be taken when administering to patients with increased bleeding tendency. Careful clinical monitoring and laboratory assessment is recommended (e.g. APTT).

Hepatic impairment (e.g. liver cirrhosis)
Clinical monitoring and laboratory assessments at regular intervals should be considered in patients with hepatic impairment as accumulation of Lornoxicam (increase in AUC) may occur after treatment with daily doses of 12-16 mg. Apart from that, hepatic impairment does not seem to affect pharmacokinetic parameters of Lornoxicam as compared to healthy subjects.

Long term treatment (longer than 3 months)
Regular laboratory assessments of hematology (hemoglobin), renal functions (creatinine) and liver enzymes are recommended.

Elderly patients above 65 years
Monitoring of renal and hepatic function is recommended. Precaution is advised in elderly postoperative patients.

Gastrointestinal bleeding, ulceration and perforation
GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time 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 hemorrhage 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 acetylsalicylic acid or other active substances likely to increase gastrointestinal risk. Clinical monitoring at regular intervals is recommended.
GI related adverse effects may be minimized by using lowest effective dose for the shortest duration necessary to control symptoms. 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 should be advised in patients receiving concomitant drugs which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as acetylsalicylic acid. The use of Lornoxicam with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided. When GI bleeding or ulceration occurs in patients receiving Lornoxicam, the treatment should be withdrawn.
The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal.

Inflammatory Bowel Disease
NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as their condition may be exacerbated.

Pre-existing Cardiovascular disease
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 edema have been reported in association with NSAID therapy.
Patients with uncontrolled hypertension, congestive heart failure, established ischemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with Lornoxicam after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipidemia, diabetes mellitus, and smoking).

Cardiovascular events
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). There are insufficient data to exclude such a risk for Lornoxicam.

Spinal/Epidural hematoma
Concomitant treatment with NSAIDs and heparin in the context of a spinal or epidural anesthesia increases the risk of spinal/epidural hematoma.

Hypersensitivity reactions
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs. Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Lornoxicam should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Prostacyclin deficiency and Nephrotoxicity
Concomitant treatment of NSAIDs and Tacrolimus may increase the risk of nephrotoxicity owing to reduced synthesis of prostacyclin in the kidney. Renal function must therefore be monitored closely in patients receiving combination therapy.

Laboratory abnormalities
As with most NSAIDs, occasional increase in serum transaminases level, increase in serum bilirubin or other liver function parameters, as well as increases in serum creatinine and blood urea nitrogen as well as other laboratory abnormalities have been reported. Should any such abnormality prove significant or persist the administration of Lornoxicam should be stopped and appropriate investigations prescribed.

Effects on fertility in women
The use of Lornoxicam, 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 who are undergoing investigation of infertility, withdrawal of Lornoxicam should be considered.

Effects on ability to drive and use machines
Patients showing dizziness and/or sleepiness under treatment with Lornoxicam should refrain from driving or operation of machinery.

ADVERSE REACTIONS

Infections and infestations

Rare: Pharyngitis.
Blood and lymphatic system disorders
Rare: Anemia, thrombocytopenia, leucopoenia, prolonged bleeding time
Very rare: Ecchymosis
Immune system disorders
Rare: Hypersensitivity.
Metabolism and nutrition disorders
Uncommon: Anorexia, weight changes.
Psychiatric disorders
Uncommon: Insomnia, depression.
Rare: Confusion, nervousness,agitation
Nervous system disorders
Common: Mild and transient headache, dizziness.
Rare: Somnolence, paraesthesia, dysgeusia, tremor, migraine.
Eye disorders
Uncommon: Conjunctivitis
Rare: Visual disturbances.
Ear and labyrinth disorders
Uncommon: Vertigo, tinnitus.
Cardiac disorders
Uncommon: Palpitations, tachycardia, edema, cardiac failure.
Vascular disorders
Uncommon: Flushing, edema.
Rare: Hypertension, hot flush, hemorrhage, hematoma.
Respiratory, thoracic and mediastinal disorders
Uncommon: Rhinitis.
Rare: Dyspnea, cough, bronchospasm.
Gastrointestinal disorders
Common: Nausea, abdominal pain, dyspepsia, diarrhea, vomiting.
Uncommon: Constipation, flatulence, eructation, dry mouth, gastritis, gastric ulcer, abdominal pain upper, duodenal ulcer, mouth ulceration.
Rare: Melena, hematemesis, stomatitis, esophagitis, gastro esophageal reflux, dysphagia, aphthous stomatitis, glossitis, perforated peptic ulcer.
Hepatobiliary disorders
Uncommon: Increase in liver function tests, SGPT (ALT) or SGOT (AST).
Rare: Hepatic function abnormal.
Very rare: Hepatocellular damage.
Skin and subcutaneous tissue disorders
Uncommon: Rash, pruritus, hyperhidrosis, rash erythematous, urticaria,alopecia
Rare: Dermatitis, purpura
Very rare: Edema and bullous reactions, Stevens-Johnson syndrome, toxic epidermal necrolysis
Musculoskeletal and connective tissue disorders
Uncommon: Arthralgia
Rare: Bone pain, muscle spasms, myalgia.
Renal and urinary disorders
Rare: Nocturia, micturition disorders, increase in blood urea nitrogen and creatinine levels.
General disorders and administration site conditions
Uncommon: Malaise, face edema.
Rare: Asthenia.

DRUG INTERACTIONS

Cimetidine
Increased plasma concentrations of Lornoxicam have been reported when Lornoxicam is used with Cimetidine. (No interaction between lornoxicam and ranitidine, or lornoxicam and antacids has been demonstrated).
Anti-coagulants
NSAIDs may enhance the effects of anti-coagulants, such as warfarin. Careful monitoring of INR/pro-thrombin time should be undertaken
Heparin
NSAIDs increase the risk of spinal or epidural hematoma when given concomitantly with heparin in the context of spinal or epidural anesthesia.
ACE inhibitors
The antihypertensive effect of the ACE inhibitor may decrease.
Diuretics
Decreased diuretic and antihypertensive effect of loop diuretics and thiazide diuretics
Beta-adrenergic blockers
Decreased antihypertensive efficacy
Digoxin
Decreased renal clearance of digoxin. Monitor digoxin levels when using Lornoxicam.
Corticosteroids
Increased risk of gastrointestinal ulceration or bleeding
Quinolone antibiotics
Increased risk of seizures with Lornoxicam
Anti-platelet agents
Increased risk of gastrointestinal bleeding
Other NSAIDs
Increased risk of gastrointestinal bleeding
Methotrexate
Increased serum concentration of methotrexate.Increased toxicity may result.When concomitant therapy has to be used careful monitoring should be undertaken.
Selective serotonin reuptake inhibitors (SSRIs)
Increased risk of gastrointestinal bleeding
Lithium
NSAIDs inhibit renal clearance of lithium, thus the serum concentration of lithium may increase above toxicity limits. Therefore serum lithium levels require monitoring, especially during initiation, adjustment and withdrawal of treatment.
Cyclosporine
Increased serum concentration of cyclosporine. Nephrotoxicity of cyclosporine may be enhanced via renal prostaglandin mediated effects. During combined treatment renal function should be monitored.
Sulphonylureas
Increased risk of hypoglycemia
Known inducers and inhibitors of CYP2C9 isoenzymes
Lornoxicam (as other NSAIDs depending on the cytochrome P450 2C9 (CYP2C9 isoenzyme)) has interactions with known inducers and inhibitors of CYP2C9 isoenzymes.
Tacrolimus
Increase the risk of nephrotoxicity owing to reduced synthesis of prostacyclin in the kidney. During combined treatment renal function should be monitored.

USE IN SPECIAL POPULATIONS

Pregnancy
Lornoxicam is contraindicated in the third trimester of pregnancy and should not be used during Pregnancy in the first and second trimesters and delivery as no clinical data on exposed pregnancies are available. There are no adequate data from the use of Lornoxicam in pregnant women. Studies in animals have shown reproductive toxicity.
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation after use of a prostaglandin synthesis inhibitor in early pregnancy. 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- fetal lethality. During the first and second trimester of pregnancy, prostaglandin synthesis inhibitors should not be given unless clearly necessary.
Prostaglandin synthesis inhibitors administered during the third trimester of pregnancy may expose the fetus to cardiopulmonary toxicity (premature closure of the ductus arteriosus and pulmonary hypertension) and renal dysfunction which may lead to renal failure and hence a reduced quantity of amniotic fluid. At the end of pregnancy, prostaglandin synthesis inhibitors may expose the mother and the fetus to increased bleeding time and inhibition of uterine contractions, which may delay or prolong the labor. Therefore, the use of Lornoxicam is contraindicated during the third trimester of pregnancy.

Nursing mothers
There are no data on the excretion of Lornoxicam in human breast milk. Lornoxicam is excreted in milk of lactating rats in relatively high concentrations. Therefore, Lornoxicam should not be used in breastfeeding women.

Pediatrics
Lornoxicam is not recommended for use in children and adolescents below age 18 due to a lack of data on safety and efficacy.

Elderly
No special dosage modification is required for elderly patients above age 65, but Lornoxicam should be administered with precaution as gastrointestinal adverse effects are less well tolerated in this group.

Renal impairment
Dosage adjustment is required in renal impairment patients. (See DOSAGE and WARNINGS & PRECAUTIONS)

Hepatic impairment
Dosage adjustment is required in hepatic impairment patients. (See DOSAGE and WARNINGS & PRECAUTIONS)

OVER DOSAGE

There is no experience of overdose to permit definition of the consequence of an overdose, or to suggest specific managements. However, it can be expected that after an overdose with Lornoxicam, the following symptoms can be seen: Nausea, vomiting, cerebral symptoms (dizziness, disturbances in vision). Severe symptoms are ataxia ascending to coma and cramps, liver and kidney damages and maybe coagulation disorders.
In the case of a real or suspected overdose, the medicinal product should be withdrawn. Due to its short half-life, Lornoxicam is rapidly excreted. Lornoxicam is not dialyzable. No specific antidote is known to date. The usual emergency measures including gastric lavage should be considered. Based on principles, only administering activated charcoal immediately after the intake of Lornoxicam can lead to diminished absorption. Gastrointestinal disorders can for example be treated with a prostaglandin analogue or ranitidine.

PRESENTATION

Spedicam 8mg: Available in the Pack of 10's Tablets.

INSTRUCTIONS

Use as advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from light, heat and moisture.
Store below 30°C.
For suspected adverse drug reaction, email us at
reports@pharmevo.biz

For more information on our products
call PharmAssist helpline 0800-82222
Monday to Friday 9:00 am to 6:00 pm
or email us at : pharmassist@pharmevo.biz

ہدایات:
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
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پیر تا جمعہ صبح 9:00 بجے تا شام 6:00 بجے
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Our dream, a healthier society

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