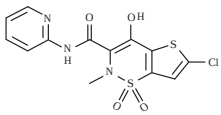
Orno® Rapid 8mg Tablets
(Lornoxicam)

DESCRIPTION:
Orno® Rapid (Lornoxicam) is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class with analgesic properties for the treatment of moderate to severe pain. Chemically it is 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. Its molecular formula is $C_{13}H_{10}ClN_3O_4S_2$ and the structural formula is:



COMPOSITION:
Orno® Rapid 8mg Tablets
Each film coated tablet contains:
Lornoxicam MS.....8mg

PHARMACODYNAMICS:
Mechanism of action
The mode of action of lornoxicam is mainly related to the inhibition of the prostaglandin synthesis (inhibition of the cyclooxygenase enzyme) leading to desensitization 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

PHARMACOKINETICS:
Absorption
Lornoxicam is absorbed rapidly and almost completely from the gastrointestinal tract. Maximum plasma concentrations are achieved after approximately 30 minutes. The absolute bioavailability of lornoxicam is 90-100%. No first-pass effect has been observed. The mean elimination half-life is 3-4 hours

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

Biotransformation
Lornoxicam is extensively metabolized in the liver, primarily to the inactive 5–hydroxylornoxicam 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 2/3 is eliminated via the liver and 1/3 via the kidneys as inactive substance

Elimination
The mean elimination half-life of the parent compound is 3 to 4 hours. After oral administration about 50% is excreted in the faeces and 42% through the kidneys, mainly as 5-hydroxylornoxicam. In elderly patients above age 65, the clearance is reduced with 30-40%. 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 16mg

INDICATIONS:
Short-term relief of acute mild to moderate pain

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

For acute pain
8 - 16mg lornoxicam given in doses of 8mg. An initial dose of 16mg followed by 8mg 12 hours later can be given on the first treatment day. After the first treatment day the maximum recommended daily dose is 16mg

OR
As directed by the physician

Additional Information on Special Populations
Children and adolescents: Lornoxicam is not recommended for use in children and adolescents below age 18 because of a lack of data on safety and efficacy

Elderly: No special dosage modification is required for elderly patients above age 65 unless renal or hepatic function is impaired. Lornoxicam should be administered with precaution as gastrointestinal adverse effects are less well tolerated in this group

Renal impairment: Reduction of dose frequency of lornoxicam to once daily in patients suffering from renal impairment is recommended

Hepatic impairment: Reduction of dose frequency of lornoxicam to once daily in patients suffering from hepatic impairment is recommended. Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms

ADVERSE REACTIONS:
The most common adverse effects of lornoxicam are nausea, dyspepsia, indigestion, abdominal pain, vomiting, diarrhea, headache and dizziness

WARNINGS AND PRECAUTIONS:
Lornoxicam should only be administered after careful risk-benefit assessment in following disorders:

Renal impairment
Lornoxicam should be administered with precaution in patients with mild (serum creatinine 150-300µmol/l) to moderate (serum creatinine 300–700µmol/l) 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
Careful clinical monitoring and laboratory assessment is recommended (e.g. APTT)

Hepatic impairment
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 12-16mg. 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

INTERACTIONS:
Concomitant administration of lornoxicam with
Cimetidine: Increased plasma concentrations of lornoxicam
Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin
Phenprocoumon: Decreased effect of phenprocoumon treatment
Heparin: NSAIDs increase the risk of spinal or epidural haematoma when given concomitantly to heparin in the context of spinal or epidural anaesthesia
ACE inhibitors: Antihypertensive effect of ACE inhibitor may decrease
Diuretics: Decreased diuretic and antihypertensive effect of loop diuretics, thiazide diuretics, and potassium sparing diuretics
Beta-adrenergic blockers: Decreased antihypertensive efficacy
Angiotensin II receptor blocker: Decreased antihypertensive efficacy
Digoxin: Decreased renal clearance of digoxin
Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding
Quinolone antibiotics: Increased risk of seizures
Anti-platelet agents: Increased risk of gastrointestinal bleeding
Other NSAIDs: Increased risk of gastrointestinal bleeding
Methotrexate: Increased serum concentration of methotrexate and increased toxicity may result
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
Sulphonylureas: Increased risk of hypoglycemia
Known inducers and inhibitors of CYP2C9 isoenzymes: Lornoxicam 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
Pemetrexed: NSAIDs may reduce renal clearance of pemetrexed resulting in increased renal and gastrointestinal toxicity, and myelosuppression. Food may decrease the absorption with about 20% and increase T_{max}

CONTRAINDICATIONS:
Lornoxicam is contraindicated in conditions like hypersensitivity reactions (symptoms like asthma, rhinitis, angioedema or urticaria), thrombocytopenia, 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, severe hepatic impairment, severe renal impairment and during pregnancy and lactation

OVERDOSAGE:
Symptoms expected after an overdose with lornoxicam are nausea, vomiting, dizziness, disturbances in vision and severe symptoms are ataxia ascending to coma and cramps, liver and kidney damages and may be 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 dialysable. 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 of the preparation. Gastrointestinal disorders can for example be treated with a prostaglandin analogue or ranitidine

STABILITY:
See expiry on the pack

PRESENTATION:
Orno® Rapid 8mg tablets in a pack of 10's

INSTRUCTIONS:
Keep out of reach of children
Avoid exposure to heat, light and humidity
Store between 15 to 30°C
Improper storage may deteriorate the medicine

اورنو® ریپڈ ۸ ملی گرام ٹیبلٹ
(لورناکسیکیم)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں

ہدایات: بچوں کی پہنچ سے دور رکھیں

دوا کو دھوپ، گرمی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ
کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی

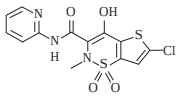
Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com

Orno® (Lornoxicam) 8mg Injection (Lyophilized)

For I.M. / I.V. use

DESCRIPTION:

Lornoxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class with analgesic properties. Chemically, it is described as 6-chloro-4-hydroxy-2 methyl-N-2-pyridinyl-2H-thieno[2,3-e][1,2]-thiazine-3-carboxamide1,1-dioxide. Its molecular formula is $C_{13}H_{10}ClN_3O_4S_2$ and the structural formula is:



It is intended for short-term treatment of acute mild to moderate pain when oral administration is inappropriate

COMPOSITION:

Orno® 8mg Injection (Lyophilized):

Each vial contains:

Lornoxicam MS.....8mg

PHARMACODYNAMICS:

Mechanism of action: The mode of action of lornoxicam is mainly related to the inhibition of the prostaglandin synthesis (inhibition of the cyclooxygenase enzyme) leading to desensitization 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

PHARMACOKINETICS:

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

Biotransformation: Lornoxicam is extensively metabolized in the liver, primarily to the inactive 5–hydroxylornoxicam 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 2/3 is eliminated via the liver and 1/3 via the kidneys as inactive substance

Elimination: The mean elimination half-life of the parent compound is 3 to 4 hours. About 50% is excreted in the faeces and 42% through the kidneys, mainly as 5-hydroxylornoxicam. In elderly patients above age 65, the clearance is reduced with 30-40%. 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 16mg

INDICATIONS:

- 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

DIRECTION FOR RECONSTITUTION:

Dissolve the content of vial in 2ml water for injection from the accompanying ampoule, immediately prior to use

DOSAGE AND METHOD OF ADMINISTRATION:

Lornoxicam 8mg Injection (Lyophilized)

Recommended dose: 8mg intravenous or intramuscular. Daily dose should not exceed 16mg. Some patients may need a further 8mg given during the first 24 hours

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

8-16mg lornoxicam daily divided into 2 or 3 doses. Maximum recommended daily dose is 16mg Osteoarthritis and Rheumatoid arthritis

Initial recommended dose is 12mg lornoxicam daily divided into 2 or 3 doses. Maintenance dose should not exceed 16 mg lornoxicam daily

OR

As directed by the physician

Additional information on special populations

Children and adolescents: Lornoxicam is not recommended for use in children and adolescents below age 18 because of a lack of data on safety and efficacy

Elderly: No special dosage modification is required for elderly patients above age 65 unless renal or hepatic function is impaired. Lornoxicam should be administered with precaution as gastrointestinal adverse effects are less well tolerated in this group

Renal impairment: Reduction of dose frequency of lornoxicam to once daily in patients suffering from renal impairment is recommended

Hepatic impairment: Reduction of dose frequency of lornoxicam to once daily in patients suffering from hepatic impairment is recommended. Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms

ADVERSE REACTIONS:

The most common adverse effects of lornoxicam are nausea, dyspepsia, indigestion, abdominal pain, vomiting, diarrhoea, headache and dizziness

WARNINGS AND PRECAUTIONS:

Lornoxicam should only be administered after careful risk-benefit assessment in following disorders:

Renal impairment: Lornoxicam should be administered with precaution in patients with mild (serum creatinine 150-300µmol/l) to moderate (serum creatinine 300 – 700µmol/l) 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: Careful clinical monitoring and laboratory assessment is recommended (e.g. APTT)

Hepatic impairment: 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

INTERACTIONS:

Concomitant administration of lornoxicam with:

Cimetidine: Increased plasma concentrations of lornoxicam

Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin

Phenprocoumon: Decreased effect of phenprocoumon treatment

Heparin: NSAIDs increase the risk of spinal or epidural haematoma when given concomitantly to heparin in the context of spinal or epidural anaesthesia

ACE inhibitors: Antihypertensive effect of ACE inhibitor may decrease

Diuretics: Decreased diuretic and antihypertensive effect of loop diuretics, thiazide diuretics, and potassium sparing diuretics

Beta-adrenergic blockers: Decreased antihypertensive efficacy

Angiotensin II receptor blocker: Decreased antihypertensive efficacy

Digoxin: Decreased renal clearance of digoxin

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding

Quinolone antibiotics: Increased risk of seizures

Anti-platelet agents: Increased risk of gastrointestinal bleeding

Other NSAIDs: Increased risk of gastrointestinal bleeding

Methotrexate: Increased serum concentration of methotrexate and increased toxicity may result

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

Sulphonylureas: Increased risk of hypoglycemia

Known inducers and inhibitors of CYP2C9 isoenzymes: Lornoxicam 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

Pemetrexed: NSAIDs may reduce renal clearance of pemetrexed resulting in increased renal and gastrointestinal toxicity, and myelosuppression

LACTATION:

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

CONTRAINDICATIONS:

Lornoxicam is contraindicated in conditions like hypersensitivity reactions (symptoms like asthma, rhinitis, angioedema or urticaria), thrombocytopenia, 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, severe hepatic impairment, severe renal impairment and during pregnancy and lactation

OVERDOSAGE:

Symptoms expected after an overdose with lornoxicam are nausea, vomiting, dizziness, disturbances in vision and 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 dialysable. No specific antidote is known to date

STABILITY:

See expiry on the pack

AVAILABILITY:

Orno® 8mg injection (Lyophilized) in a pack of 1 vial + 2ml sterile water for injection

INSTRUCTIONS:

Keep out of reach of children

Avoid exposure to heat, light and humidity

Store between 15 to 30°C

Improper storage may deteriorate the medicine

اورنو® ۸ ملی گرام انجکشن (لائیوفلائیزڈ)

(لورناکسیکیم)

برائے عضلاتی / وریدی استعمال

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں

ہدایات: بچوں کی پہنچ سے دور رکھیں

دوا کو دھوپ، گرمی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com

R.N-01/HA/05/18