TENOVIX

Instructions for the medicinal product

Composition:
Combipack contains 3 vials & 3 ampoules.
Each vial contains:
Tenoxicam BP 20 mg
Each ampoule contains:
Sterile water for injection BP 2 ml

Product Description:
Physical properties: Yellow coloured lyophilized cake filled in 2 ml clear glass vial.
Chemical name: Tenoxicam
Molecular weight: 337.37414 g/mol
Empirical / Structural formula: $C_{13}H_{11}N_3O_4S_2$

ATC Classification: M01AC02.

Pharmacologic property:
Pharmacodynamics:
Tenoxicam is a non-steroidal anti-inflammatory drug which has marked anti-inflammatory and analgesic activity and some antipyretic activity. Tenoxicam contains the substance with the approved name tenoxicam. It is chemically described as 4-hydroxy-2-methyl-N-(pyridin-2-yl)-2H-thieno-[2,3-e]1,2-thiazine-3-carboxamide 1, 1-dioxide. As with other non-
steroidal anti-inflammatory drugs, the precise mode of action is unknown, though it is probably multifactorial, involving inhibition of prostaglandin biosynthesis and reduction of leucocyte accumulation at the inflammatory site.
Pharmacokinetics:
Tenoxicam is long-acting; a single daily dose is effective. Tenoxicam penetrates well into synovial fluid to give concentrations approximately half those in plasma. The mean plasma elimination half-life is approximately 72 hours. Following intravenous administration of 20 mg tenoxicam, plasma levels of the drug decline rapidly during the first two hours mainly due to distribution processes. Following intramuscular injection levels at or above 90% of the maximally achieved concentrations are reached as early as 15 minutes after a dose.
With the recommended dosage regimen of 20 mg once daily, steady-state plasma concentrations are reached within 10-15 days, with no unexpected accumulation. Tenoxicam is strongly bound to plasma proteins. Tenoxicam is cleared from the body almost exclusively by metabolism. Approximately two-thirds of the administered dose is excreted in the urine, mainly as the pharmacologically inactive 5-hydroxypyridyl metabolite, and the remainder in the bile, much of it as glucuronide conjugates of hydroxyl-metabolites.
No age-specific changes in the pharmacokinetics of tenoxicam have been found although inter-individual variation tends to be higher in elderly persons.

Indication:
- For the relief of pain and inflammation in osteoarthritis and rheumatoid arthritis;
- for the short term management of acute musculoskeletal disorders including strains, sprains and other soft-tissue injuries.
- For the management of postoperative pain.

IV, IM Tenovix can be used for these indications in those patients considered unable to take oral Tenovix .

Recommended Dose Mode of Administration:
Adults:
Tenovix should be given IV or IM. A single daily dose of 20 mg for one to two days initially to be continued with the oral form, with administration at the same time each day. The lyophilisate should be dissolved in 2 ml of sterile water for injections and the reconstituted solution should be used immediately.
Higher doses should be avoided as they do not usually achieve significantly greater therapeutic effect but may be associated with a higher risk of adverse events.
In acute musculoskeletal disorders treatment should not normally be required for more than 7 days, but in severe cases it may be continued up to a maximum of 14 days.
Use in the elderly:
As with other non-steroidal anti-inflammatory drugs, Tenovix should be used with special caution in elderly patients. The elderly are at increased risk of serious adverse reactions. They are also more likely to be receiving concomitant medication or to have impaired hepatic, renal or cardiovascular function. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.
Children:
There are insufficient data to make a recommendation for administration of Tenovix to children.
Use in renal and hepatic insufficiency:
Creatinine clearance -Greater than 25 mL/min. Dosage regimen -Usual dosage but monitor patients carefully.
Creatinine clearance - Less than 25 mL/min Dosage regimen - Insufficient data to make dosage recommendations.
Because of the high plasma protein-binding of tenoxicam, caution is required when plasma albumin concentrations are markedly reduced (e.g. in nephrotic syndrome) or when bilirubin concentrations are high.
There is insufficient information to make dosage recommendations for Tenovix in patients with pre-existing hepatic impairment.

Contraindications:
- Hypersensitivity to tenoxicam or to any of the excipients;
- Patients who have previously shown hypersensitivity reactions (symptoms of asthma, rhinitis, angioedema or urticaria) to other NSAIDs, including ibuprofen and aspirin, as the potential exists for cross-sensitivity to tenoxicam.
- Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding), ulcerative colitis, Crohn's disease, severe gastritis, or history of gastrointestinal bleeding or perforation, related to previous NSAID therapy.
- Severe heart failure, hepatic failure and renal failure.
- Last trimester of pregnancy.

Warnings and Precautions:
The use of Tenovix with concomitant NSAIDs including COX-2 selective inhibitors should be avoided. Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms.
The elderly have an increased frequency of adverse reactions to NSAIDs especially GI bleeding and perforation which may be fatal. Particular care should be taken to regularly monitor elderly patients to detect possible interactions with concomitant therapy and to review renal, hepatic and cardiovascular function which may be potentially influenced by NSAIDs.
Effects on ability to drive and use machines:
None.

Interactions with Other medicaments:
Anticoagulants: Tenoxicam is highly bound to serum albumin, and can, as with all NSAIDs, enhance the anticoagulant effect of warfarin and other anticoagulants. Close monitoring of the effects of anticoagulants and oral glycaemic agents is advised, especially during the initial stages of treatment with Tenoxicam Lyophilisate.
Antiplatelet agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding.
Antihypertensive: Tenoxicam and other NSAIDs can reduce the effects of anti-hypertensive drugs.
Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels when co-administered with cardiac glycosides.
Ciclosporin: As with all NSAIDs caution is advised when ciclosporin is co-administered because of the increased risk of nephrotoxicity.
Cimetidine: No interaction has been found with concomitantly administered cimetidine.
Corticosteroids: As with all NSAIDs, caution should be taken when co-administering corticosteroids because of the increased risk of GI ulceration or bleeding.
Diuretics: Reduced diuretic effect. NSAIDs may cause sodium, potassium and fluid retention and may interfere with the natriuretic action of diuretic agents, which can increase the risk of nephrotoxicity of NSAIDs.
Lithium: NSAIDs have been reported to decrease elimination of lithium. If tenoxicam is prescribed for a patient receiving lithium therapy, the frequency of lithium monitoring should be increased, the patient warned to maintain fluid intake and to be aware of symptoms of lithium intoxication.
Methotrexate: Caution is advised where methotrexate is givenconcurrently because of possible enhancement of its toxicity, since NSAIDs have been reported to decrease elimination of methotrexate.
Mifepristone: NSAIDs should not be used for 8 - 12 days after mifepristone administration as NSAIDs can reduce the effects of mifepristone.
NSAIDs, COX-2 Selective Inhibitors, Salicylates: Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects.
Penicillamine and parenteral gold: No clinically relevant interaction was found in small numbers of patients receiving treatment with penicillamine or parenteral gold.
Quinolones: Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.
Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.
Zidovudine: Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV positive
haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Pregnancy and Lactation:
The safety of Tenovix during pregnancy and lactation has not been established and the drug should therefore not be given in these conditions. In view of the known effects of NSAIDs on the foetal cardiovascular system (risk of closure of the ductus arteriosus), use in the last trimester of pregnancy is contraindicated.
NSAIDs can appear in the breast milk in very low concentrations. NSAIDs should, if possible, be avoided when breastfeeding.

Undesirable Effects:
Cardiovascular and cerebrovascular: oedema, hypertension, and cardiac failure, have been reported in association with NSAID treatment. Palpitations and dyspnoea have been reported rarely.
Dermatological: Photosensitivity and bullous reactions including Stevens - Johnson syndrome and Toxic Epidermal Necrolysis (very rare) have been reported.
Gastrointestinal: The most common side-effects relate to the GI tract. They include dyspepsia, nausea, vomiting, abdominal pain and discomfort, constipation, diarrhoea, flatulence, indigestion, epigastric distress, melaena, haematemesis, ulcerative stomatitis, anorexia, exacerbation of colitis and Crohn's disease.
Hematological: Decreases in haemoglobin, unrelated to gastro-intestinal bleeding, have occurred. Anaemia, aplastic anaemia, haemolytic anaemia, thrombocytopenia and non-thrombocytopenic purpura, leucopenia, neutropenia and eosinophilia have been reported. Epistaxis has been reported infrequently. Rare cases of agranulocytosis have been reported.
Hepatic: Abnormal liver function. As with most other NSAIDs, changes in various liver function parameters have been observed. Some patients may develop raised serum transaminase levels during treatment. Although such reactions are rare, if abnormal liver function tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop or if systemic manifestations occur (e.g. eosinophilia, rash), Tenovix should be discontinued. Hepatitis and jaundice have also been reported.
Hypersensitivity: Hypersensitivity reactions have been reported following treatment with NSAIDs, these include:
Non specific allergic reactions and anaphylaxis; Respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea assorted skin disorders; incl. rashes of various types. Angioedema, pruritus, and purpura have been reported. Nail disorders, alopecia, erythema, urticaria, and photosensitivity reactions have been reported rarely. As with other NSAIDs, exfoliative and bullous dermatoses, incl. epidermal necrolysis, erythema multiform and Stevens-Johnson syndrome may develop in rare instances. Vesiculo - bullous reactions and vasculitis have also been reported rarely.
Metabolism: Metabolic abnormalities, such as weight decrease or increase and hyperglycaemia, have occurred rarely. Neurological and special senses: Visual disturbances, optic neuritis, swollen eyes, blurred vision and eye irritation have been reported. Ophthalmoscopy and slit-lamp examination have revealed no evidence of ocular changes. Malaise and tinnitus may occur.
Other less common reports include: Paraesthesia, aseptic meningitis (especially in patients with existing auto-immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation, dizziness, malaise, fatigue and drowsiness. Headache, somnolence, insomnia, depression, nervousness, dream abnormalities, mental confusion, paraesthesias and vertigo have been reported rarely.
Renal: Nephrotoxicity has been reported in various forms, including interstitial nephritis, nephrotic syndrome and renal failure. Reversible elevations of blood urea nitrogen and creatinine have been reported.

Overdose and Treatment:
Symptoms: there is no reported experience of serious overdosage with Tenovix. Symptoms of NSAID overdose include headache, nausea, vomiting, epigastric pain, GI bleeding, rarely diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, fainting, occasionally and convulsions. In cases of significant poisoning acute renal failure and liver damage are possible.
Treatment: patients should be treated symptomatically as required. Good urine output should be ensured. Renal and liver function should be closely monitored. Patients should be observed for at least four hours after a potentially toxic dose. Frequent or prolonged convulsions should be treated with intravenous diazepam. Administration of H2 antagonist drugs may be of benefit. Other measures may be indicated by the patient's clinical condition.

Dosage Forms and Packaging Available:
3+3, 3 vial of 2ml Lyophilized and 3 ampoule of 2 ml for WFI

Storage:
Keep in dry place protected from light at a temperature below 30°C. Keep out of reach of children.

Shelf life:
2 years. Do not use after expiry date.

Distribution Condition:
Prescription only medicine (POM).

Manufactured for:
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