NEW ZEALAND DATA SHEET

1. PRODUCT NAME

TENOXICAM Devatis Powder for Injection, 20 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Each vial contains 20 mg Tenoxicam.
Reconstituted Tenoxicam Devatis solution contains 10 mg/ml tenoxicam.

Excipient(s):
For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Vial containing lyophilized powder for injection
Yellow-green colored lyophilized mass

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Tenoxicam Devatis is indicated in adults for the symptomatic treatment of the following painful inflammatory and degenerative disorders of the musculoskeletal system:

- rheumatoid arthritis
- osteoarthritis
- arthrosis
- ankylosing spondylitis
- extra-articular disorders, e.g. tendinitis, bursitis, periarthritis of shoulders (shoulder-hand syndrome) or hips, strains and sprains
- post-operative pain

4.2 Posology and method of administration

Posology/frequency and duration of administration
Undesirable effects may be minimized by using the lowest effective dose for the shortest possible duration necessary to control symptoms (see section 4.4).
For all indications except post-operative pain, a daily single dose of 20 mg should be administered at the same time of day.
For post-operative pain the recommended dose is 40 mg daily for 5 days.
In treatment of chronic disorders the therapeutic effect of tenoxicam is evident early in treatment and there is a progressive increase in response over time. In chronic disorders, daily doses higher than 20 mg are not recommended since this would increase the frequency and intensity of unwanted reactions without significantly increasing efficacy.
For patients needing long-term treatment a reduction to a daily oral dose of 10 mg may be tried for maintenance (this cannot be achieved using this product, i.e. a tablet presentation should be used).

Method of administration
The lyophilized power in the vial should be dissolved in 2 ml of sterile water for injection. The prepared solution should be administered by intramuscular (IM) or intravenous (IV) bolus injection immediately.
Where indicated, treatment is initiated with single dose by IV or IM administration daily for one or two days

and continued tenoxicam given by oral or rectal route.
Lyophilized powder for injection is developed for IM or IV bolus administration; due to possibility of precipitation it should not be used by infusion.

Additional information regarding special populations

Renal impairment
The above dosage recommendations also apply to patients with renal impairment. However, it is recommended that when tenoxicam is used in patients with renal impairment, kidney functions should be carefully monitored. Dosage should be minimised in patients with renal impairment. It should not be used in patients with severe renal impairment.

Hepatic impairment
The above dosage recommendations also apply to patients with hepatic impairment. However, it is recommended that when tenoxicam is used in patients with hepatic impairment, liver functions should be carefully monitored. Dosage should be minimised in patients with hepatic impairment. It should not be used in patients with severe hepatic impairment**.**

Pediatric population
No dosage recommendations have been established for children and adolescents due to insufficient data. Not to be used in this age group.

Geriatric population
The elderly have an increased risk of gastrointestinal bleeding, ulceration or perforation which may be fatal. These patients should commence treatment on the lowest dose available and combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients who are using concurrent and also for patients requiring concomitant low dose salicylates, or other drugs likely to increase gastrointestinal risk (see section 4.4).

4.3 Contraindications
Tenoxicam Devatis is contraindicated in:
- Patients with a known hypersensitivity to tenoxicam or any of the excipients in combination of Tenoxicam Devatis or to other non-steroidal anti-inflammatory drugs (NSAIDs).
- Patients who have previously shown symptoms of asthma, rhinitis, angioedema or urticaria due to salicylates or other non-steroidal anti-inflammatory drugs (NSAIDs).
- Patients with active or with a history of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy (see section 4.4).
- Patients with active or history of recurrent peptic ulcer or hemorrhage (two or more distinct episodes of proven ulceration or bleeding) (see section 4.4).
- Hemorrhagic diathesis, as with other NSAIDs.
- As with other NSAIDs, in patients with severe heart failure, renal failure and hepatic failure.
- Last trimester of pregnancy (see section 4.6)

4.4 Special warnings and precautions for use
Tenoxicam Devatis is relatively contraindicated in patients with liver dysfunction.
The use of tenoxicam with concomitant NSAIDs, including cyclo-oxygenase-2 selective inhibitors should be avoided.
Because of the high plasma protein-binding of tenoxicam, when plasma albumin concentrations are markedly reduced, care and precaution should be taken.
Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and GI bleeding, ulceration and perforation).

Cardiovascular and cerebrovascular effects

Appropriate monitoring is 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. Clinical trial and epidemiological data suggest that use of selective COX-2 inhibitors and some NSAIDs (particularly at high doses and long term treatment) may be associated with an increased risk of arterial thrombotic events, including myocardial infarction and stroke, which may increase with dose or duration of use. Patients with cardiovascular disease or cardiovascular risk factors may also be at greater risk.

Patients with uncontrolled hypertension, congestive heart failure, established ischemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with Tenoxicam Devatis 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, smoking).

To minimize the potential risk of an adverse cardiovascular event in patients taking an NSAID, especially in those with cardiovascular risk factors, the lowest effective dose should be used for the shortest possible duration (see section 4.2).

NSAIDs may lead to the onset of new hypertension or worsening of pre-existing hypertension and patients taking anti-hypertensives with NSAIDs may have an impaired anti-hypertensive response.

Caution is advised when prescribing NSAIDs to patients with hypertension. Blood pressure should be monitored closely during initiation of NSAID treatment and at regular intervals thereafter.

Fluid retention and oedema have been observed in some patients taking NSAIDs; therefore, caution is advised in patients with fluid retention or heart failure.

There is no consistent evidence to suggest that concurrent use of aspirin mitigates the possible increased risk of serious cardiovascular thrombotic events associated with NSAID use.

Gastrointestinal bleeding, ulceration and perforation:
GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs including Tenoxicam Devatis at any time during treatment, with or without warning symptoms or a previous history of serious GI events. Studies have not identified any subset of patients not at risk of developing peptic ulcer and bleeding.

Upper gastrointestinal ulcers, gross bleeding or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3 - 6 months and in about 2 - 4% of patients treated for one year. These trends continue with longer duration of use, increasing the likelihood of developing a serious gastrointestinal event at some time during the course of therapy. However, even short term therapy is not without risk.

Caution is advised in patients with risk factors for gastrointestinal events who may be at greater risk of developing serious gastrointestinal events e.g. the elderly, those with a history of serious gastrointestinal events, smoking and alcoholism.

The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation, which may be fatal. Debilitated patients do not seem to tolerate ulceration or bleeding as well as others. Most of the fatal gastrointestinal events associated with NSAIDs occurred in the elderly and/or debilitated patients. 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 hemorrhaged or perforation (see section 4.3) and in the elderly.

Patients with risk factors should commence treatment on the lowest dose available and combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients who are using concurrent and also for patients requiring concomitant low dose salicylates, or other drugs

likely to increase gastrointestinal risk (see below and section 4.5).

NSAIDs should be given with care to patients with a history of inflammatory bowel disease (ulcerative colitis; Crohn's disease) as their condition may be exacerbated. Patients with a history of gastrointestinal toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding) particularly in the initial stages of treatment. If peptic ulceration or gastrointestinal bleeding occurs, Tenoxicam Devatis should be withdrawn immediately. Physicians should warn patients about the signs and symptoms of serious gastrointestinal toxicity.

Caution is advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or antiplatelet agents such as salicylates (see section 4.5).

Skin reactions
Life-threatening cutaneous reactions such as exfoliative dermatitis, toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS), which can be fatal and occur without warning, have been reported with tenoxicam. These serious adverse effects are idiosyncratic and are independent of dose or duration of use.

Patients should be advised of the signs and symptoms of serious skin reactions and monitored closely for skin reactions. The highest risk of occurrence of SJS or TEN is within the first weeks of treatment.

If symptoms or signs of SJS or TEN (e.g. progressive skin rash often with blisters of mucosal lesions) are present, Tenoxicam Devatis should be discontinued. The best results for managing SJS and TEN come from early diagnosis and immediate discontinuation of any suspected drug. Early withdrawal is associated with a better prognosis.

If the patient has developed SJS or TEN with the use of tenoxicam, tenoxicam must not be restarted in this patient at any time.

Hematologic effects
Tenoxicam inhibits platelet aggregation and may affect hemostasis. Tenoxicam Devatis has no significant influence on blood coagulation factors, coagulation time, prothrombin time and activated thromboplastin time.

Patients having coagulation disorders or receiving therapy that interferes with hemostasis should, however, be carefully observed when Tenoxicam Devatis is administered.

Ocular effects
Adverse eye findings have been reported with NSAIDs including Tenoxicam Devatis. Thus ophthalmic evaluation is recommended for patients who develop visual disturbances.

Antipyretic effects
As known for other anti-inflammatory medicines, Tenoxicam Devatis may mask the usual signs of infection.

Renal impairment
NSAIDs inhibit renal prostaglandin synthesis and consequently may have an undesirable effect on renal hemodynamics and on salt and water balance. It is necessary to adequately monitor the patient with a special emphasis on cardiac and renal function (BUN, creatinine, development of edema, weight gain, etc.) in patients with history of renal disease, impaired renal function in diabetics, hepatic cirrhosis, congestive heart failure, hypovolemia and concomitant treatment with potentially nephrotoxic medicines, diuretics and corticosteroids. This group of patients is at special risk in peri- and post-operative phases of major surgery due to the possibility of serious blood loss. They therefore require close monitoring in the postoperative and recovery periods.

Because of the high plasma protein binding of tenoxicam, caution is required when plasma albumin levels are markedly reduced.

4.5 Interaction with other medicinal products and other forms of interaction

Acetylsalicylate and salicylates
Salicylates increase the clearance and volume of distribution of NSAIDs including tenoxicam and decrease the mean minimum steady-state plasma concentrations of tenoxicam by displacing them from protein binding sites. Concurrent treatment with salicylates or other NSAIDs is not recommended because of increased risk of undesirable reactions.

Anti-platelet agents and selective serotonin reuptake inhibitors
Concomitant use of anti-platelet agents and selective serotonin-reuptake inhibitors (SSRIs) with NSAIDs increases the risk of gastrointestinal bleeding (see section 4.4)

Methotrexate
The co-administration of some NSAIDs and methotrexate has been associated with reduced renal tubular secretion of methotrexate, higher plasma concentrations of methotrexate, and severe methotrexate toxicity. Therefore, caution should be exercised when Tenoxicam Devatis is administered concurrently with methotrexate.

Lithium
As tenoxicam may decrease the renal clearance of lithium, their concomitant administration may lead to increased plasma levels and toxicity of lithium. The plasma levels of lithium should be closely monitored.

Diuretics and anti-hypertensives
As with NSAIDs in general, tenoxicam should not be administered concurrently with potassium sparing diuretics. There is a known interaction between these two classes of compounds, which may cause hyperkalemia and renal failure.
No clinically significant interaction between tenoxicam and furosemide was noted, but tenoxicam attenuates the blood pressure lowering effect of hydrochlorothiazide. As known from other NSAIDs, tenoxicam might attenuate the antihypertensive effects of alpha-adrenergic blockers and ACE-inhibitors.
There was no clinically relevant interaction when tenoxicam was administered together with atenolol. During clinical trials no interaction was reported for patients treated concomitantly with digitalis products. Thus concurrent dosing of Tenoxicam Devatis and digitalis products appears to be without major risk.

Antacids and H_2-receptor blockers
No clinically relevant interaction has been found with concomitantly administered antacids and cimetidine at the recommended dosages.

Probenecid
Co-administration of probenecid and tenoxicam treatment may increase plasma concentration of tenoxicam. The clinical significance of this observation has not been established.

Anticoagulants
No clinically relevant interaction has been found with concomitantly administered warfarin and phenprocoumon, and low molecular weight heparin at the recommended dosages. Nevertheless, as for other NSAIDs, careful monitoring is recommended when patients concomitantly receive anticoagulants.

Oral Antidiabetics
The clinical effect of the oral antidiabetic medicines glibornuride, glibenclamide and tolbutamide was likewise not modified by tenoxicam. Nevertheless, as for other NSAIDs, careful monitoring is recommended when patients concomitantly receive oral antidiabetic drugs.

Colestyramine
Colestyramine may increase the clearance and reduce the half-life of tenoxicam.

Dextromethorphan
The concomitant administration of tenoxicam and dextromethorphan may increase the analgesic effect compared to monotherapy.

Ciclosporin
Increased risk of nephrotoxicity.

Alcohol
There is no significant pharmacodynamic interaction between tenoxicam and alcohol but concomitant use of alcohol with tenoxicam enhances the gastric mucosa damage.

4.6 Fertility, Pregnancy and Lactation

General principles
Pregnancy category is C/D (3.trimester)

Women of childbearing potential/Contraception
There is no data regarding the effects of tenoxicam on birth control (contraception). The use of tenoxicam, as with any agent known to inhibit cyclooxygenase/prostaglandin synthesis, may impair fertility and is not recommended in women attempting to conceive. If it is used by a woman attempting to conceive, the dose should be kept as low and duration of treatment as short as possible.

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-fetal 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, Tenoxicam Devatis should not be given unless clearly necessary. If Tenoxicam Devatis 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 fetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension)
- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis

And 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 labor.

Consequently, Tenoxicam Devatis is contraindicated during the third trimester of pregnancy.

Breastfeeding
Based on findings from single dose administration, a very small amount (mean value less than 0.3% of the dose) of tenoxicam passes into breast milk (see section 5.2).
There is no evidence of adverse reactions in breast-fed infants of mothers taking tenoxicam. Nevertheless, infants should be weaned or the medicine discontinued.

Fertility
The use of tenoxicam, as with any agent 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 fertility, withdrawal of tenoxicam treatment should be considered (see section 5.3).

4.7 Effects on ability to drive and use machines
Patients experiencing adverse events that might affect driving or using machines, such as vertigo, drowsiness or visual disturbances should refrain from driving a car or using machines.

4.8 Undesirable effects
Based on clinical trials including large numbers of patients, tenoxicam proved to be well tolerated in the recommended dose. Usually the undesirable effects reported were mild and transient. In a small proportion of patients the interruption of treatment due to undesirable effects was necessary.
Local tolerance of parenteral administration of tenoxicam was found to be good.

The most commonly observed adverse events in association with NSAIDs are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, melena, hematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following NSAIDs administration. Less frequently, gastritis has been observed.

Following terms and frequencies are used for undesirable effects due to tenoxicam use:
Very common (≥1/10) common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10000, <1/1000), very rare (<1/10000), not known (cannot be estimated from the available data).

Blood and lymphatic system disorders
Not known: Anemia, agranulocytosis, leucopenia, thrombocytopenia.

Immune system disorders
Not known: Hypersensitivity reactions such as dyspnea, asthma, anaphylaxis, angioedema.

Metabolism and nutrition disorders
Uncommon: Decreased appetite

Psychiatric disorders
Uncommon: Sleep disorder
Not known: Confusional state, Hallucinations

Nervous system disorders
Common: Dizziness, headache
Not known: Paresthesia, Somnolence

Eye disorders
Not known: Visual disturbances (such as visual impairment and vision blurred)

Ear and labyrinth disorders
Uncommon: Vertigo

Cardiac disorders
Uncommon: Palpitations
Not known: Cardiac failure

Vascular disorders
Not known: Vasculitis.
Clinical trials and epidemiological data suggest that use of selective cyclooxygenase 2 inhibitors (COX2 inhibitors) and some NSAIDs (particularly at high doses and long term treatment) may be associated with a slight increase in risk of arterial thrombotic event (e.g. myocardial infarction or stroke).
Although tenoxicam has not shown to increase thrombotic events such as myocardial infarction, there are insufficient data to exclude such a risk with tenoxicam.

Gastrointestinal disorders
Common: Gastric, epigastric and abdominal pain, dyspepsia, nausea
Uncommon: Gastrointestinal bleeding (including hematemesis and melena), Gastrointestinal ulcer, Constipation, Diarrhea, Vomiting, Mouth ulceration, Gastritis, Dry mouth.
Very rare: Pancreatitis
Not known: Gastrointestinal perforation, Exacerbation of colitis and Crohn's disease, Flatulence

Hepatobiliary disorders
Uncommon: Increased hepatic enzymes
Not known: Hepatitis

Skin and subcutaneous tissue disorders
Uncommon: Pruritus, erythema, exanthema, rash, urticaria.
Very rare: Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome),
Not known: Photosensitivity reactions.

Renal and urinary disorders
Uncommon: Increased blood urea or creatinine

Reproductive system and breast disorders
Not known: Female infertility
Isolated cases of female infertility have been reported with agents known to inhibit cyclooxygenase/ prostaglandin synthesis including tenoxicam.

General disorders and administration site conditions
Uncommon: Fatigue, edema

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose
Symptoms
In general, patients with a NSAID overdosage are asymptomatic. NSAID overdosage causes only minor CNS or gastrointestinal disturbances.
There have been isolated reports of more serious toxicity after ingestion of substantial quantities; they include seizures, coma and renal failure, and cardio-respiratory arrest may occur. Hepatic dysfunction, hypothrombobinemia and metabolic acidosis are also reported.

Treatment
In case of overdosage appropriate supportive treatment is indicated and discontinuation of the medicine, antacids and proton-pump inhibitors may be indicated. There are no known specific antidotes. Dialysis does not significantly clear NSAIDs from the blood stream.

For further advice on management of overdose please contact the National Poisons Information Centre (0800

POISON or 0800 764 766).

Drug abuse and dependence: Drug dependency, addiction and recreational abuse have not been reported as a problem with this compound.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antirheumatic, anti-inflammatory and analgesic agent.
ATC code: M01AC02

The active ingredient of Tenoxicam Devatis, tenoxicam, is a non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic and anti-rheumatic properties and it also inhibits platelet aggregation. Tenoxicam inhibits prostaglandin biosynthesis by inhibition of cyclooxygenase 1 (COX-1) and 2 (COX-2), both *in vitro* (sheep seminal vesicles) and *in vivo* (protection of arachidonic acid-induced toxicity in mice).
In vitro investigation on cyclooxygenase isoenzymes prepared from human COS-7 cells have shown that tenoxicam inhibits COX-1 and COX-2 isoenzymes approximately to the same extent i.e. COX-2/COX-1 ratio equals to 1.34.
In vitro tests of leukocyte peroxidase suggest that tenoxicam may act as a scavenger for active oxygen at the site of inflammation.
Tenoxicam is a potent *in vitro* inhibitor of human metalloproteinases (stromelysin and collagenase) which induce cartilage breakdown.
A further possible mechanism of action is the reduction of nitrite levels indicating an alteration of NO pathways.
These pharmacological effects explain, at least in part, the therapeutic benefit of Tenoxicam Devatis in the treatment of painful inflammatory and degenerative disorders of the musculoskeletal system.

5.2 Pharmacokinetic properties

General properties
Absorption:
Following intramuscular administration bioavailability is complete and there is no difference between oral administrations. 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 conditions are reached within 10-15 days without unexpected accumulation. The average concentration at steady state is 11 mg/L when tenoxicam is given at oral doses of 20 mg once daily and this does not change even on treatment for up to 4 years.
As predicted from single dose kinetic, plasma concentrations at steady state are 6-fold higher than those reached after a single dose.

Distribution:
Following intravenous administration of 20 mg tenoxicam, plasma levels of the drug decline rapidly during the first 2 hours mainly due to distribution processes. The average distribution volume at steady state is 10-12 L.
In the blood over 99% of the medicine is bound to albumin. Tenoxicam penetrates well into the synovial fluid. Peak concentrations are reached later than in plasma.
Based on findings from single dose administration a very small amount (mean value less than 0.3% of the dose) of tenoxicam passes into breast milk (see section 4.6).

Metabolism:
Tenoxicam is excreted via liver after virtually complete biotransformation to pharmacologically inactive metabolites.

Elimination:
Up to two thirds of the administered dose is excreted in the urine (mainly as the inactive 5'-hydroxy-tenoxicam) and the rest via the bile (a significant portion in the form of glucuronidated compounds). Not more than 1% of the administered dose is excreted unchanged via urine. The mean elimination half-life of tenoxicam is 72 hours (range 59 to 74 hours). The total plasma clearance is 2 ml/min.

Linearity/nonlinearity:
The pharmacokinetics of tenoxicam is linear in the investigated dose range of 10 to 100 mg.

Characteristics in patients

Renal impairment:
Studies in patients with renal impairment suggest that no dose adjustment is necessary to achieve plasma concentrations similar to those seen in healthy subjects.

Liver impairment:
Studies in patients with liver impairment suggest that no dose adjustment is necessary to achieve plasma concentrations similar to those seen in healthy subjects.

Geriatric population:
Studies in the elderly suggest that no dose adjustment is necessary to achieve plasma concentrations similar to those seen in healthy subjects. The kinetic profile in the elderly is observed as similar to healthy subjects.

Other:
The kinetic profile in patients with rheumatic disease is observed as similar to healthy subjects.
Because of the high plasma protein binding of tenoxicam, caution is required when plasma albumin levels are markedly reduced (see section 4.4).

5.3 Preclinical safety data

Carcinogenicity: Tenoxicam showed no carcinogenic effects in animals.

Mutagenicity: Tenoxicam showed no mutagenic effects in animals.

Impairment of fertility:
The use of tenoxicam, as with any agent known to inhibit cyclooxygenase/prostaglandin synthesis, may impair fertility and is not recommended in women attempting to conceive. In women who have difficulty conceiving or are undergoing investigation of infertility, withdrawal of tenoxicam treatment should be considered.

Teratogenicity: Tenoxicam showed no teratogenic effects in animals.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Ascorbic Acid
Disodium edetate
Mannitol
Sodium hydroxide
Trometamol
Hydrochloric acid (for pH adjustment)

6.2 Incompatibilities
TENOXICAM Powder for Injection should not be used with infusions due to risk of precipitation.
In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life
24 months. Tenoxicam Devatis product should be used immediately after reconstitution.

6.4 Storage conditions
Store at or below 30°C protected from light.

6.5 Type and nature of container
Colorless 3 ml glass vial, which contains 20 mg lyophilized mass.

6.6 Special precautions for disposal and other handling
Any unused material should be disposed according to local disposal regulations.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

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9. DATE OF FIRST APPROVAL

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Date of latest renewal:

10. DATE OF REVISION OF THE TEXT

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