PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr] TENOXICAM

Tenoxicam Tablets

Tablets, 20 mg and Oral

House Standard

Anti-inflammatory, Analgesic Agent

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RECENT MAJOR LABEL CHANGES

2 Contraindications	08/2022
3 Serious Warnings and Precautions Box	08/2022
7 Warnings and Precautions	08/2022
7 Warnings and Precautions, 7.1.1 Pregnant Women	08/2022

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

TENOXICAM (tenoxicam tablets) is indicated for the:

- symptomatic treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and extra-articular inflammations such as tendinitis, bursitis and periarthritis of the shoulders or hips.

1.1 Pediatrics

Pediatrics (< 16 years): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of TENOXICAM in pediatric patients has not been established; therefore, Health Canada has not authorized an indication for pediatric use. (See 7.1.3. Pediatrics)

1.2 Geriatrics

Geriatrics: Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness.

2 CONTRAINDICATIONS

- TENOXICAM is contraindicated during the third trimester of pregnancy, because of risks of premature closure of the ductus arteriosus, and prolonged parturition.
- TENOXICAM should not be administered to patients with active peptic ulcer or active inflammatory diseases of the gastrointestinal tract. TENOXICAM is contraindicated in patients who have shown hypersensitivity to the drug.
- Tenoxicam should not be used in patients in whom acute asthmatic attacks, urticaria, rhinitis or other allergic manifestations are precipitated by acetylsalicylic acid (ASA) or other nonsteroidal anti-inflammatory agents. Fatal anaphylactoid reactions have occurred in such individuals.
- Before anesthesia or surgery, TENOXICAM should not be given to elderly patients, to patients at risk of renal failure, or to patients with increased risk of bleeding, because of an increased risk of acute renal failure and possibility of impaired hemostasis.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- Peptic ulcerations, perforation and gastrointestinal bleeding, sometimes severe and occasionally fatal have been reported during therapy with nonsteroidal anti-inflammatory drugs (NSAIDs) including tenoxicam.
- Patients taking any NSAID including this drug should be instructed to contact a physician immediately if they experience symptoms or signs suggestive of peptic ulceration or gastrointestinal bleeding. These reactions can occur without warning symptoms or signs and at any time during the treatment.
- **Risk in Pregnancy:** Caution should be exercised in prescribing TENOXICAM during the first and second trimesters of pregnancy. Use of NSAIDS at approximately 20 weeks of gestation or later may cause fetal renal dysfunction leading to oligohydramnios and neonatal renal impairment or failure (see 7 WARNINGS AND PRECAUTIONS). TENOXICAM is contraindicated for use during the third trimester because of risk of premature closure of the ductus arteriosus and uterine inertia (prolonged parturition) (see 2 CONTRAINDICATIONS).

4 DOSAGE AND ADMINISTRATION

4.2 Recommended Dose and Dosage Adjustment

- A single daily dose of 20 mg TENOXICAM should be taken orally at the same time each day. Higher doses should be avoided as they do not usually achieve a significantly greater therapeutic effect, but may be associated with a higher risk of adverse events.
- In some patients, a 10 mg (1/2 tablet) daily dose may be sufficient. The smallest effective dose should be prescribed.
- Use in Elderly:
  As with other NSAIDs, TENOXICAM should be used with special caution in elderly patients since they may be less able to tolerate side effects than younger patients. They are also more likely to be receiving concomitant medication or to have impaired hepatic, renal or cardiovascular function.

4.5 Missed Dose

If you miss a dose, take the missed dose as soon as you remember. If it is almost time for your next dose, wait until then to take your medicine and skip the missed dose. Do not take two doses at the same time.

5 OVERDOSAGE

Cases of overdose with tenoxicam have not been reported. In the event of overdosage with TENOXICAM, supportive and symptomatic therapy is indicated.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Oral	Tablet 20 mg	Carnauba wax, colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polydextrose, polyethylene glycol, titanium dioxide and yellow ferric oxide

TENOXICAM (tenoxicam) 20 mg tablets are yellow, oval, biconvex, film-coated tablets engraved "2" partial bisect "0" on one side, other side plain. Available in bottles of 100, 250, 500 and 1000 tablets.

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

General

Caution should be exercised when a NSAID such as tenoxicam is used in patients with a history suggestive of peptic ulcer, melena or any gastrointestinal disease. In these cases, the physician must weigh the benefits of treatment against the possible hazards.

Infection

In common with other anti-inflammatory drugs, TENOXICAM may mask the usual signs of infection.

Gastrointestinal

If peptic ulceration or gastrointestinal bleeding occur in patients under treatment with TENOXICAM (tenoxicam), the drug should be immediately withdrawn.

There is no definitive evidence that the concomitant administration of histamine H_2-receptor antagonists and/or antacids will either prevent the occurrence of gastrointestinal side effects or allow continuation of TENOXICAM therapy when and if these adverse reactions appear.

Hematologic

Drugs inhibiting prostaglandin biosynthesis do interfere with platelet function to some degree; therefore, patients who may be adversely affected by such an action should be carefully observed when TENOXICAM is administered.

Blood dyscrasias associated with the use of nonsteroidal anti-inflammatory drugs are rare, but could be with severe consequences.

Hepatic/Biliary/Pancreatic

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of one or more liver tests may occur. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of more severe hepatic reactions while on therapy with this drug. Severe hepatic reactions including jaundice and cases of fatal hepatitis have been reported with this drug as with other nonsteroidal anti-inflammatory drugs. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g. eosinophilia, rash, etc.), this drug should be discontinued.

During long-term therapy, liver function tests should be monitored periodically.

Monitoring and Laboratory Tests

Reversible elevation of BUN and serum creatinine have been reported with tenoxicam. The effect is thought to result from inhibition of renal prostaglandin synthesis resulting in changes in medullary and deep cortical blood flow with an attendant effect on renal function. Patients with impaired renal function or on diuretics, as well as elderly patients and those with congestive heart failure or liver ascites, are more at risk.

During long-term therapy, kidney function should be monitored periodically.

Pregnancy: If TENOXICAM is administered in the middle (approximately 20 weeks) to the end of the second trimester, it is recommended that pregnant women on TENOXICAM be closely monitored for amniotic fluid volume since TENOXICAM may result in reduction of amniotic fluid volume and even oligohydramnios (see 7.1 Special Populations). TENOXICAM is contraindicated for use in the third trimester of pregnancy.

Ophthalmologic

Blurred and/or diminished vision has been reported with the use of tenoxicam and other nonsteroidal anti-inflammatory drugs. If such symptoms develop, this drug should be discontinued and an ophthalmologic examination performed; ophthalmic examination should be carried out at periodic intervals in any patient receiving this drug for an extended period of time.

Renal

As with other nonsteroidal anti-inflammatory drugs, long-term administration of tenoxicam to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with hematuria, proteinuria, and occasionally nephrotic syndrome.

A second form of renal toxicity has been seen in patients with prerenal conditions leading to the reduction in renal blood flow or blood volume, where the renal prostaglandins have a supportive role in the maintenance of renal perfusion. In these patients, administration of a nonsteroidal anti- inflammatory drug may cause a dose-dependent reduction in prostaglandin formation and may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, and the elderly. Discontinuation of nonsteroidal anti-inflammatory therapy is usually followed by recovery to the pre-treatment state.

Fluid and Electrolyte Balance

Fluid retention and edema have been observed in patients treated with tenoxicam. Therefore, as with many other nonsteroidal anti-inflammatory drugs, the possibility of precipitating congestive heart failure in elderly patients or those with compromised cardiac function should be borne in mind. TENOXICAM should be used in caution in patients with heart failure, hypertension or other conditions predisposing to fluid retention.

With NSAID treatment, there is a potential risk of hyperkalemia particularly in patients with conditions such as diabetes mellitus or renal failure; elderly patients; and patients receiving concomitant therapy with β-adrenergic blockers, angiotensin-converting enzyme inhibitors or some diuretics. Serum electrolytes should be monitored periodically during long-term therapy, especially in those patients at risk.

Sensitivity/Resistance

As with other NSAIDs, allergic reactions may occur. Manifestation of allergic reactions include urticaria, bronchospasm and anaphylaxis.

Skin

Serious skin reactions: Use of some NSAIDs, such as TENOXICAM, have been associated with rare post-market cases of serious, fatal or otherwise life-threatening skin reactions, including:

- drug reaction with eosinophilia and systemic symptoms (DRESS)
- Stevens-Johnson syndrome
- toxic epidermal necrolysis (or Lyell's Syndrome),
- exfoliative dermatitis
- erythema multiforme

Patients appear to be at higher risk for these events early in the course of therapy, with the onset of cases usually occurring within the first month of treatment. These reactions may be reversible if the causative agent is discontinued and appropriate treatment instituted. Patients should be advised that they should discontinue their NSAID at the first appearance of a skin rash, mucosal lesions or any other sign of hypersensitivity, and contact their physician immediately for assessment and advice, including which therapies to discontinue.

DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection, and eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident.

7.1 Special Populations

7.1.1 Pregnant Women

The safety of TENOXICAM during pregnancy has not been established and therefore its use during pregnancy is not recommended.

No teratogenic effects were observed in animal reproductive studies. Rats receiving tenoxicam during pregnancy showed delayed delivery. Tenoxicam readily passes into the milk of lactating rats.

TENOXICAM is contraindicated for use during the third trimester of pregnancy because of risks of premature closure of the ductus arteriosus and the potential to prolong parturition (see 16 NON-CLINICAL TOXICOLOGY). Caution is recommended in prescribing TENOXICAM during the first and second trimesters of pregnancy, particularly from the middle to end of the second trimester of pregnancy (onset at approximately 20 weeks) due to possible fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment or failure.

Published studies and postmarketing reports describe maternal NSAID use at approximately 20 weeks gestation or later in pregnancy associated with fetal renal dysfunction leading to oligohydramnios, and in some cases, neonatal renal impairment or failure. NSAIDs were shown to cause significant reduction in fetal urine production prior to reduction of amniotic fluid volume. There have also been a limited number of case reports of maternal NSAID use and neonatal renal dysfunction and renal impairment without oligohydramnios, some of which were irreversible, even after treatment discontinuation.

These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Complications of prolonged oligohydramnios may for example, include limb contractures and delayed lung maturation. In some postmarketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.

If after careful consideration of the benefit-risk, NSAID treatment is considered necessary to be administered anywhere from the middle (onset at approximately 20 weeks) to the end of the second trimester of pregnancy, the use should be limited to the lowest effective dose and shortest duration possible. It is also recommended that ultrasound monitoring of amniotic fluid be considered if TENOXICAM treatment extends beyond 48 hours and that NSAIDs treatment be discontinued if oligohydramnios occurs, followed by appropriate medical follow up.

Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or 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.

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 organogenesis period.

7.1.2 Breast-feeding

The safety of TENOXICAM during lactation has not been established and therefore its use during lactation is not recommended.

7.1.3 Pediatrics

TENOXICAM is not recommended for use in patients under 16 years of age, as the dose and indications in this population have not been established.

7.1.4 Geriatrics

Elderly, frail and debilitated patients appear to be at higher risk from a variety of adverse reactions from nonsteroidal anti-inflammatory drugs (NSAIDs). As with other nonsteroidal anti-inflammatory drugs, TENOXICAM (tenoxicam) should be used with special caution in these patients.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The most common adverse reactions encountered with nonsteroidal anti-inflammatory drugs are gastrointestinal, of which peptic ulcer, with or without bleeding, is the most severe. Fatalities have occurred on occasion, particularly in the elderly.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

In approximately 12,000 patients administered tenoxicam 10 - 40 mg/day (approximately four-fifths receiving 20 mg/day), the incidence of peptic ulceration and the incidence of gastrointestinal bleeding (including hematemesis and melena) was 0.1 - 0.6%.

The approximate incidences of other adverse effects listed by systems are summarized below:

Gastrointestinal (10.4 - 23.0%): Dyspepsia (0.1-9.7%), nausea (2.0-6.7%), constipation (0.5-2.9%), abdominal pain (0.7-3.3%), diarrhea (0.5-2.3%), flatulence (0.04-1.9%), vomiting (0.2-1.1%), ulcerative stomatitis (0.1-0.7%), gastritis (0.1-0.8%), esophagitis (0.2%), abdominal discomfort (1.4-2.2%), pyrosis (1.3-1.9%), epigastric discomfort (0.2-0.4%), epigastric pain (1.8-2.5%), hyperacidity (0.02-0.4%), anorexia (0.05-0.4%), indigestion (0.1-0.2%), meteorism (0.2-0.4%), gastric pressure (0.5-1.0%), mouth dryness (0.1-0.3%). Glossitis, stomatitis, dysphagia and reflux esophagitis were each reported in less than 0.1% of the patients.

Dermatologic (1.6 - 3.9%): Rash (0.2-1.4%), pruritus (0.3-1.3%), sweating (0.06-0.3%), exanthema (0.2-0.3%), itching (0.05-0.4%). Photosensitivity reaction, seborrhea, urticaria, eczema and nail disorder were each reported in 0.1% or less of the patients. One case of angioedema was also reported.

Central Nervous System (2.0 - 9.1%): Headache (0.9-4.3%), dizziness (0.8-3.3%), malaise (0.04-0.8%), paresthesia (0.02-0.5%), somnolence (0.1-0.7%), vertigo (0.2-0.4%), confusion (0.2%),

fatigue (0.1-0.9%), depression (0.6%), insomnia (0.1-0.2%). Leg cramps, nervousness, fever and paresis were each reported in 0.1% of the patients.

Cardiovascular: Hypertension (0.02-0.3%), palpitations (0.02-0.2%), flushing (0.02-0.03%), purpura (0.02-0.2%). Tachycardia was reported in less than 0.1% of the patients.
Hematologic: Anemia (0.04-0.3%), leukopenia (0.04-0.4%). Thrombocytopenia was reported in 0.1% or less of the patients.

Renal: Hematuria (0.02 - 0.2%), edema (0.2-1.3%), micturition frequency (0.02-0.3%), polyuria (0.03-0.1%). Dysuria, cystitis, increased BUN, increased creatinine, and albuminuria were each reported in less than 0.1% of the patients. Isolated cases of abnormal renal function and one case of renal failure were reported.

Hepatic (0.06-0.4%): Abnormal hepatic function (0.3%). Jaundice, increased SGOT, SGPT, gamma GT and bilirubin were each reported in less than 0.1% of the patients. Hepatitis, hepatic coma and hepatic failure were each reported once.

Respiratory (0.02-0.65%): Dyspnea (0.2%), bronchospasm (0.1%).

Eyes, Ears, Nose, Throat:

Vision abnormal (0.02-0.3%). Diplopia, conjunctivitis, tinnitus, deafness, epistaxis, abnormal lacrimation were each reported in 0.1% or less of the patients.

Skin

Serious skin reactions: Use of some NSAIDs, such as TENOXICAM, have been associated with rare post-market cases of serious, fatal or otherwise life-threatening skin reactions, including:

- drug reaction with eosinophilia and systemic symptoms (DRESS)
- Stevens-Johnson syndrome
- toxic epidermal necrolysis (or Lyell's Syndrome),
- exfoliative dermatitis
- erythema multiforme

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

Acetylsalicylic Acid or Other NSAIDs: Plasma concentrations of tenoxicam are reduced to approximately 80% of their normal concentrations when single doses of tenoxicam are administered in conjunction with acetylsalicylic acid (2,600 to 3,900 mg/day). At steady state, simultaneous administration of ASA does not appear to have a significant effect on the plasma concentration of tenoxicam. The use of TENOXICAM in conjunction with acetylsalicylic acid or other nonsteroidal anti-inflammatory agents is not recommended since data are not available demonstrating that the combination produces greater improvement than that achieved with either drug alone, and the potential for adverse reactions is increased.

Protein-Bound Drugs: As with other NSAIDs, TENOXICAM is highly protein-bound, and therefore, might be expected to displace other protein-bound drugs, such as anticoagulants, oral hypoglycemics (sulfonylureas), phenytoin and sulfonamides.

Short-term pharmacodynamic studies have demonstrated that tenoxicam does not potentiate the anticoagulant effect of coumarin-type anticoagulants nor the hypoglycemic effect of sulfonylurea drugs. However, when a NSAID such as TENOXICAM is administered concomitantly with anticoagulants, oral hypoglycemics, or other highly protein-bound drugs, the patient should be monitored and dosage adjustments made, if necessary.

Diuretics/Antihypertensives: As with other nonsteroidal anti-inflammatory drugs, TENOXICAM can attenuate the blood pressure lowering effect of hydrochlorothiazide and the peak excretion rates of Na^+ and Cl^- in patients with hypertension. Therefore, close monitoring of patients on this drug combination is advisable. The excretion of electrolytes was not significantly affected when tenoxicam (two-day loading dose of 40 mg daily, followed by 20 mg daily) was administered to normotensive patients receiving furosemide therapy (40 mg daily).

Some NSAIDs have been reported to reduce the antihypertensive effects of certain β-blockers. The interaction between TENOXICAM and β-blockers has not been studied.

Digoxin: In elderly patients with normal plasma creatinine levels, plasma digoxin levels were not altered by the concomitant administration of tenoxicam (30 mg daily).

Antacids: The administration of 15 mL of an aluminum hydroxide or an aluminum and magnesium hydroxide antacid just prior to a single 20 mg oral dose of tenoxicam did not affect the bioavailability of tenoxicam.

Cholestyramine: The average half-life of tenoxicam, after a single 20 mg intravenous dose, was reduced from 67.4 hours to 31.9 hours following the administration of cholestyramine (4 g in 200 mL water p.o. t.i.d.). The apparent drug clearance of tenoxicam increased by 105%.

Lithium: Nonsteroidal anti-inflammatory agents have been reported to increase steady state plasma lithium concentrations. It is recommended that these concentrations be monitored when initiating, adjusting and discontinuing TENOXICAM treatment.

Methotrexate: The co-administration of some NSAIDs and methotrexate has been associated with reduced renal tubular secretion of methotrexate, higher plasma concentrations, and severe methotrexate toxicity. Therefore, caution should be exercised when NSAIDs, such as TENOXICAM, are administered concurrently with methotrexate. The interaction between tenoxicam and methotrexate has not been studied.

9.5 Drug-Food Interactions

Interactions with food have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Tenoxicam is a nonsteroidal anti-inflammatory agent with analgesic and antipyretic properties. Its mechanism of action, as with other nonsteroidal anti-inflammatory agents, is not yet completely known. Tenoxicam is an inhibitor of prostaglandin biosynthesis both *in vitro* and *in vivo* (protects mice against arachidonic acid induced toxicity). *In vitro* tests of leukocyte peroxidase also suggest that tenoxicam may act as a scavenger for active oxygen at the site of inflammation. These effects probably explain in part, the activity of tenoxicam in the treatment of painful inflammatory and degenerative diseases of the musculoskeletal system. Tenoxicam does not act by pituitary- adrenal stimulation.

After 4, 7, 10 or 14 days of culture with tenoxicam (2.4, 12, 48 mcg/mL), there was no significant effect on the amount of cartilage proteoglycans synthesized and released into the culture medium of human chondrocytes, as compared to untreated cultures.

In vitro studies have also shown that tenoxicam inhibits the activity of both proteoglycanase and collagenase enzymes obtained from human osteoarthritic cartilage. These *in vitro* results suggest a positive effect of tenoxicam on the joint cartilage under experimental conditions by slowing down the enhanced catabolism of the osteoarthritic cartilage matrix. The clinical significance of these findings is not yet known and is being investigated.

10.2 Pharmacodynamics

Tenoxicam has anti-inflammatory, analgesic and antipyretic properties as shown in various pharmacological models.

Anti-Inflammatory Activity

The anti-inflammatory activity of orally-administered tenoxicam was determined in rats. Administration of a 30 mg/kg dose of tenoxicam produced a 50% reduction of carrageenan-induced paw edema. Administration of oral doses of the drug (0.3 to 3 mg/kg) caused inhibition of the acute inflammatory response (Days 0 to 4) of adjuvant-induced arthritis in rats. At the development stage, administration of the same amount of drug inhibited the development of arthritis. In the cotton pellet-induced granuloma test, tenoxicam (ED_{30} 8.2 mg/kg), piroxicam and indomethacin were approximately equipotent inhibitors of granuloma formation.

Analgesic Activity

The analgesic activity of tenoxicam in the phenylquinone-induced writhing test was compared to that of piroxicam, indomethacin and naproxen in rats. The analgesic potencies of tenoxicam, piroxicam and naproxen were similar ($ED_{50} \cong 1$ mg/kg), while that of indomethacin was considerably less (ED_{50} 17 mg/kg). Tenoxicam at doses of 1.25 to 20 mg/kg was active in the Randall-Sellito test in which painful pressure is applied to the inflamed foot pads of rats.

Tenoxicam was inactive in the hot plate test (ED_{50} >300 mg/kg).

Antipyretic Activity

The antipyretic activity was shown in hyperetic rats. Following subcutaneous injection of a yeast suspension, the ED_{50} for tenoxicam (0 to 5 hours) was 1.7 mg/kg.

Tenoxicam is a potent inhibitor of prostaglandin and thromboxane synthesis due to its inhibition of fatty acid cyclooxygenase. No difference was seen between the activity of tenoxicam and indomethacin in the inhibition of arachidonic acid-induced platelet aggregation, which is mediated by the interaction of the formed thromboxane A_2 and the prostaglandin E_2 with their specific receptors. Tenoxicam inhibits platelet aggregation with greater potency than acetylsalicylic acid (ASA), but in contrast to ASA, the inhibition is reversible. Platelet adhesion is not affected.

As a consequence of the inhibition of gastric prostaglandin synthesis, tenoxicam, like other NSAIDs, may cause gastrointestinal side effects such as ulcers and gastrointestinal bleeding.

In vitro tests of leukocyte peroxidase suggest that tenoxicam may act as a scavenger for oxygen derived free radicals at the site of inflammation.

As with other NSAIDs, tenoxicam inhibits to a certain extent renal excretion of water and electrolytes in the rat (but not in the dog). The perinatal and postnatal study of tenoxicam showed that it has the potential to inhibit uterine contraction, with the increased incidence of dystocia and delayed parturition, as of all cyclooxygenase inhibitors.

Further studies in mice, rats, rabbits, cats, dogs and monkeys indicate that tenoxicam is devoid of effects on the cardiovascular, respiratory, central and autonomic nervous systems at doses higher than needed for the anti-inflammatory or analgesic response. Tenoxicam does not influence weight of the thymus or the adrenal glands in rats.

10.3 Pharmacokinetics

Absorption

Tenoxicam is extensively absorbed following oral administration with an absolute bioavailability of approximately 100%. Following a single oral dose of a 20 mg tablet, peak plasma concentrations (1.46 to 3.31 mcg/mL) were reached within one-half hour to six hours (median: 1.25 hours), and the mean half-life was 72 ± 28 hours (range: 32-110 hours) in eight fasted healthy males. When taken with a meal, tenoxicam is absorbed to the same extent but at a slower rate (peak plasma concentration is attained after four hours).

Distribution:

Following multiple doses of 20 mg once daily, steady-state conditions are reached within 10 - 15 days. Maximum steady-state plasma concentrations fall within the range of 10 - 15 mcg/mL. An average of 17% (4.8 - 45.3%) of a 20 mg oral dose is found in the bile as the C-7 or C-8 0-glucuronide of tenoxicam.

In 14 elderly patients suffering from osteoarthritis or rheumatoid arthritis, the mean peak plasma concentration after a single 20 mg dose of tenoxicam was 2.6 mcg/mL, and the mean maximum steady-state plasma concentration after multiple dosing was 12.4 mcg/mL.

Tenoxicam is highly bound to the albumin component of plasma proteins (98-99%).

Total tenoxicam concentrations in synovial fluid were determined in six patients (three male, three female) after receiving a single 40 mg oral dose of tenoxicam. Peak synovial concentrations (1.82 mcg/ mL) were reached after 10 hours. The area under the synovial fluid tenoxicam concentration-time curve was 40-50% of the area under the plasma tenoxicam concentration-time curve.

Over a 2-week period of observantion, six healthy volunteers taking tenoxicam 20 mg daily in a single dose, showed significantly less mean daily fecal blood loss (5.71 mL/week) than they did when taking 1.2 - 3.0 g of acetylsalicylic acid daily (9.41 mL/week).

Metabolism:

Animal Metabolism

The pharmacokinetic profile of tenoxicam was determined in rats and dogs. The drug is completely and rapidly absorbed after oral administration to rats and dogs. In rats, radioactivity in the blood attained 70 - 90% of peak plasma concentrations within 15 minutes after oral administration. Very similar plasma-time profiles were seen in dogs after oral administration of ^{14}C-tenoxicam. In both rats and dogs, a biphasic decline of blood concentrations of tenoxicam was observed.

A significant sex difference for the elimination of tenoxicam was observed in Sprague-Dawley rats after a single oral dose of radioactive tenoxicam. In males, the elimination half-life was 3.4 hours and 17.5 hours for the first and second phase, respectively. In females, the half-lives were 7.2 and 21.2 hours, respectively.

The distribution of the drug was extensive in both species. In rats and dogs, the drug is eliminated from the body through hepatic metabolism. After a single oral (5 mg/kg) administration of ^{14}C- tenoxicam to male albino rats, approximately 85% of the drug was excreted in 48 hours; 50% in the feces and 35% in the urine. Similar excretion patterns of tenoxicam and its metabolites were seen in beagle dogs.

Human Metabolism

Due to the relatively rapid absorption and the long elimination half-life of tenoxicam, plasma concentration-time profiles after oral and intravenous administration were similar. The absolute bioavailability for the oral drug indicated complete absorption in the unchanged form.

The mean amounts of radioactivity in the feces and urine were 11% and 48%, respectively, 120 hours after administration of a 40 mg oral dose of tenoxicam. Urine collection up to 300 hours after dosing indicated that two-thirds of the oral dose might ultimately be excreted in the urine.

When 20 mg/day was administered orally for 18 days, only tenoxicam and 5-hydroxytenoxicam could be identified and quantified in plasma. At steady state, the concentrations of the metabolite in plasma were only 0.5 - 2% of the corresponding tenoxicam concentrations.

In the urine, 15 - 39% of the administered dose was found as the 5-hydroxy metabolite, whereas the renal excretion of unchanged tenoxicam was only 0.16 - 0.4% of the dose. A small percentage (2.6%) of the dose was excreted as the 5-hydroxytenoxicam glucuronide.

Elimination

Approximately two-thirds of a single 40 mg oral dose of tenoxicam is excreted in the urine, mainly as inactive 5'hydroxy-tenoxicam (20-30%). Only small amounts of the unchanged drug (0.5%) were found in the urine.

Special Populations and Conditions

- **Sex:** The sex-dependent difference in the disposition of tenoxicam was investigated. There was no difference in the maximum plasma concentrations, whereas a difference, at the 0.10 level of significance, was seen for the time to reach maximum drug concentrations (3.6 hours for males, 1.52 hours for females), and for the half-life of elimination (72.4 hours for males and 61.8 hours for females).

- **Hepatic Insufficiency:** In four male and two female patients with liver cirrhosis, the mean peak plasma concentration was 2.6 mcg/mL and the half-life of elimination ranged between 26 - 84 hours after a single 20 mg dose of tenoxicam.

- **Renal Insufficiency:** In eight male and four female patients with renal insufficiency (creatinine clearance 6-57 mL/min), peak plasma concentrations were in the range of 1.2 - 5.2 mg/mL and the half-life of elimination ranged from 30 - 110 hours after a single 20 mg dose of tenoxicam. Pharmacokinetic parameters in patients with renal insufficiency were not significantly different from those in healthy volunteers.

11 STORAGE, STABILITY AND DISPOSAL

Store at room temperature 15°C to 30°C.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

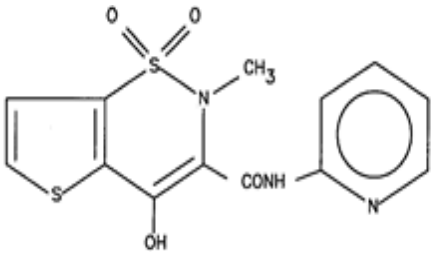
Drug Substance

Proper name: Tenoxicam

Chemical name:
1) 2*H*-Thieno[2,3-*e*]-1,2-thiazine-3-carboxamide,4-hydroxy-2-methyl- *N*-2-pyridinyl-, 1,1-dioxide;
2) 4-Hydroxy-2-methyl-N-2-pyridyl-2H-thieno[2,3-e]-1,2- thiazine-3-carboxamide 1,1-dioxide.

Molecular formula and molecular mass: $C_{13}H_{11}N_3O_4S_2$ and 337.37 g/mol

Structural formula:



Physicochemical properties: Tenoxicam is a yellow, practically odourless crystalline powder, which melts (with decomposition) at approximately 219°C- 221°C. The pk_a values are approximately 1.1 and 5.3. Tenoxicam is quite insoluble in water and common organic solvents. The solubility in 95% ethanol at 25°C is approximately 0.05 g/100 mL. The solubility at 37°C in water is approximately 0.01 g/100 mL, in artificial gastric juice (pH 1.2) approximately 0.01 g/100 mL and in artificial intestinal juice (pH 7.5) approximately 0.42 g/100 mL.

Product Characteristics:

Each TENOXICAM tablet contains 20 mg tenoxicam. In addition, TENOXICAM tablets also contain the following non-medicinal ingredients: colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polydextrose, polyethylene glycol, titanium dioxide, yellow ferric oxide and carnauba wax.

14 CLINICAL TRIALS

14.3 Comparative Bioavailability Studies

A randomized, two way, single dose (2 x 20 mg), crossover comparative bioavailability study of TENOXICAM (AA Pharma Inc.) and Mobiflex (Hoffman-La Roche Ltd.) was conducted in healthy, adult, male subjects under fasting conditions. The results obtained from the 19 subjects that were included in the statistical analysis are presented in the following table.

SUMMARY TABLE OF THE COMPARATIVE BIOAVAILABILITY DATA

Tenoxicam (2 x 20 mg) Geometric Mean Arithmetic Mean (CV%)				
Parameter	Test[1]	Reference[2]	% Ratio of Geometric Means	90% Confidence Interval
$AUC_{0\text{-}72h}$ (mcg•h/mL)	238.70 242.58 (16.9)	233.78 237.77 (17.5)	102.1	99.2 – 105.1
C_{max} (mcg/mL)	5.79 5.86 (15.5)	6.09 6.20 (16.2)	95.1	90.8 – 99.6
T_{max}[3] (h)	1.50 (0.67 – 4.0)	1.00 (0.33 – 2.00)		

[1] TENOXICAM (tenoxicam) tablet, 20 mg (AA Pharma Inc.)
[2] Mobiflex (tenoxicam) tablet, 20 mg (Hoffman-La Roche Ltd.), purchased in Canada
[3] Expressed as median (range)
Due to the long elimination half-life of tenoxicam, AUC_I and $T_{1/2}$ could not be accurately calculated from the data obtained in this study.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: Acute Toxicity

Species	Route	LD_{50} in mg/kg (95% confidence interval)	
		24 hours after administration	10 days after administration

Species	Route	LD_{50}in mg/kg (95% confidence interval)	
		24 hours after administration	10 days after administration
Mice	p.o i.v. i.p	771 (717-829) 340 (314-368) 523 (478-571)	460 (373-567) 340 (314-368) 523 (478-571)
Rats	p.o. i.v. i.p.	1019 (856-1214) 325 (302-349) 401 (347-465)	586 (507-677) 325 (302-349) 401 (347-465)

Toxic effects observed in animals included: yellow discolouration of urine, body weight loss, apathy, diarrhea, fecal blood loss, gastrointestinal erosions, ulceration of the mucous membranes and renal papillary necrosis.

Chronic Toxicity

Rats (80 Weeks): Tenoxicam was administered orally to rats (35/sex/ group) at daily doses of 0, 1, 3 and 6 mg/kg/day. Because of continuously increasing plasma levels and associated side effects, dosing of all groups was suspended from week 39 to 44. The 1 mg/kg/day dose was well tolerated. At 3 mg/kg/day some females presented gastrointestinal mucosal erosions and renal papillary necrosis. Six mg/kg/day caused gastrointestinal erosions and papillary necrosis. The female rats of this group had to be sacrificed after 52 weeks, presenting with gastrointestinal ulceration and renal papillary necrosis.

Baboons (12 Months): Groups of four baboons/sex/group received tenoxicam orally at doses of 1, 4 and 20 mg/kg/day. Due to adverse effect on growth, dosing in the 20 mg/kg/ day group was suspended from week 24 to 28.

One mg/kg/day was well tolerated. One baboon receiving 4 mg/kg/day was positive for occult blood. Twenty mg/kg/day produced a slightly reduced growth rate and food intake, persistent blood loss and slightly reduced red blood counts. One baboon had a repeated history of gastrointestinal infections with campylobacter and was sacrificed.

Carcinogenicity: The carcinogenicity of tenoxicam was studied in mice (51/sex/group) at doses of 0, 1, 3 or 5 mg/kg/day for 80 consecutive weeks, and in rats (50/sex/group) at doses of 0, 1, 3 and 6 mg/kg/day for 104 weeks. There was no evidence of carcinogenicity.

Genotoxicity: Investigations in three bacterial systems and four eukaryotic test systems did not reveal any mutagenic potential of tenoxicam.

Reproductive and Developmental Toxicology: Male and female rats received 0, 2, 4 or 8 mg tenoxicam daily. The males were dosed for at least 63 days prior to mating and the females

from 14 days prior to mating to 7 days after mating. The drug had no effect on male fertility or female pregnancy.

At the high dose (8 mg) there was a significant decrease in the number of corpora lutea and implantations resulting in fewer numbers of live fetuses.

TERATOLOGY STUDIES

Mice: Groups of female mice were given 0, 1, 2, 4 or 8 mg/kg tenoxicam orally daily from day 6 to day 15 of gestation. There were no drug-related adverse effects on fetuses or neonates. The functional behaviour of F_1mice was not altered.

Rats: Groups of female rats were given 0, 1, 2, 4, 8 or 12 mg/kg/day tenoxicam orally. The animals were dosed from day 7 to day 17 of gestation. A higher mortality rate was observed in the dams administered 8 (27%) or 12 mg/kg/day (65%).

All dead dams had panperitonitis with gastric lesions characteristic of NSAIDs and uterine hemorrhage. In dams which delivered naturally, drug-related gastrointestinal lesions were also seen in the 8 mg/kg/day group.

Teratogenic effects were not observed and the drug had no effect on the functional behaviour of F_1rats.

Rabbits: Groups of female rabbits were administered 0, 2, 4, 8, 16 or 32 mg/kg/day tenoxicam orally from day 6 to day 18 of gestation. The number of resorptions was significantly increased in the high dose group. Tenoxicam had no teratogenic effect at the doses tested.

Juvenile Toxicity: Groups of 20 female rats were given 0, 0.25, 0.5, 1.0 or 2 mg/kg/day orally from day 18 of gestation throughout lactation. All animals had a dose-dependent significant prolongation of gestation. The neonatal viability was dose-dependently reduced at doses of 0.5 mg/kg/day or more.

Tenoxicam at doses of 2 mg/kg/day or less had no effect on the reproductive performance or functional behaviour of female rats.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr] TENOXICAM

Tenoxicam Tablets

Read this carefully before you start taking **TENOXICAM** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **TENOXICAM**.

Serious Warnings and Precautions

- Non-steroid anti-inflammatory drugs (NSAIDS), including TENOXICAM, can cause severe side effects that can in some cases lead to death, such as:
  - Stomach ulcers,
  - Gastrointestinal perforation (a hole in the wall of your stomach or bowels), and
  - Gastrointestinal bleeding (bleeding anywhere along the GI tract between mouth and anus)
- Stop taking this medicine immediately if you develop a gastrointestinal perforation or gastrointestinal bleeding. Contact your health care professional immediately. These side effects can occur suddenly and at any time during your treatment. The symptoms and signs of these side effects are listed in the "Serious side effects and what to do about them table" box. It is found later in this leaflet.
- **Pregnancy:**
  DO NOT take TENOXICAM if you are pregnant and in a later stage of pregnancy (28 weeks or later). If you are pregnant and in an earlier stage of pregnancy (less than 28 weeks) only take TENOXICAM if you are told to do so by your doctor. Medicines like TENOXICAM may cause harm to you and your baby. Your doctor will need to closely monitor your health and that of your baby (including your amniotic fluid levels) if they prescribe TENOXICAM during this time.

What is TENOXICAM used for?

- TENOXICAM is a nonsteroidal, anti-inflammatory agent. It is used to relieve symptoms such as inflammation, swelling, fever, stiffness and joint pain, often caused by certain types of arthritis.
- TENOXICAM is not recommended for use in children less than 16 years of age.
- TENOXICAM has been prescribed to you. It should not be given to other people or used for other problems unless specified by your doctor.

How does TENOXICAM work?

- TENOXICAM works by interfering with the production of compounds in the body that cause pain and inflammation.

What are the ingredients in TENOXICAM?

Medicinal ingredients: Tenoxicam

Non-medicinal ingredients: Carnauba wax, colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polydextrose, polyethylene glycol, titanium dioxide and yellow ferric oxide.

TENOXICAM comes in the following dosage forms:

Tablets: 20 mg

Do not use TENOXICAM if:

- you are allergic to tenoxicam or any of the other ingredients of this medicine
- you have a history of stomach problems
- you have had any unusual or allergic reactions with other nonsteroidal anti-inflammatory agents or ASA (acetylsalicylic acid) related products
- you are an elder and will been given anesthesia or have surgery
- you have a history of kidney disease or at increased risk of bleeding
- you are pregnant and in a later stage of pregnancy (28 weeks or later).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take TENOXICAM. Talk about any health conditions or problems you may have, including if you:

- have a history of stomach ulcer or bleeding
- have a history of kidney or liver disease
- are presently taking medications to relieve your symptoms of arthritis.
- have edema (increased water retention in tissues)
- have a heart failure
- have high blood pressure
- have diabetes
- are taking antihypertensive drugs like β-blockers, angiotensin-converting enzyme inhibitors or some diuretics
- have blood related problems
- are pregnant, planning on becoming or become pregnant while taking TENOXICAM.

- are breast-feeding.
- are weak

Other warnings you should know about:

Tell your doctor, dentist or pharmacist that you consult or see, that you are taking this medication.

Breastfeeding: You should not take TENOXICAM if you are breastfeeding. It is not known if TENOXICAM passes into breast milk.

Serious Skin Reactions: In rare cases, serious or life-threatening skin reactions listed below have been reported with some NSAIDs, such as TENOXICAM.

- Drug reaction with eosinophilia and systemic symptoms (DRESS)
- Stevens-Johnson syndrome (SJS),
- toxic epidermal necrolysis (TEN),
- exfoliative dermatitis and
- erythema multiforme

You may be at a greater risk of experiencing a serious skin reaction usually during the first month of treatment. Stop taking TENOXICAM and contact your doctor **right away** if you experience any of the following symptoms at any time during treatment with TENOXICAM:

- fever
- severe rash
- blisters or peeling skin
- swelling of the face
- swollen lymph glands
- flu-like feeling
- yellow skin or eyes
- shortness of breath
- swelling of the legs
- dry cough
- chest pain or discomfort
- feeling thirsty
- urinating less often, less urine or dark urine

Infection: TENOXICAM may mask the usual signs of an infection.

Vision: Blurred and/or reduced vision has been reported with some NSAIS including TENOXICAN. Stop taking TENOXICAM if you develop symptoms of blurred or reduced vision and seek medical attention right away.

Allergic Reactions: Allergic reactions have occurred during treatment with TENOXICAN. Stop taking this medicine immediately if you develop the symptoms of allergic reactions including rashes, trouble breathing and wheezing (bronchospasm) and anaphylaxis.

Driving and Using Machines: Give yourself time to see how you feel before driving a vehicle or using machinery. Blurred or reduced vision and being dizzy or drowsy can occur.

Elderly Patients: Elderly patients may be at a greater risk of developing certain side effects.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with TENOXICAM:

- Acetylsalicylic Acid or Other NSAIDS (used for inflammation, pain, fever)
- Anticoagulants (used to stop blood clotting)
- Oral anti diabetic drugs (sulfonylureas)
- Phenytoin (used to treat fits/epilepsy)
- Sulfonamides (for infections)
- A diuretic (water pills) like hydrochlorothiazide, furosemide for high blood pressure
- β-blockers for high blood pressure
- Digoxin (for heart problems)
- Antacids like aluminum hydroxide, magnesium hydroxide (used to treat conditions such as indigestion, heartburn)
- Cholestyramine (used to treat high cholesterol)
- Lithium (for mental health problems)
- Methotrexate (used to treat skin problems, arthritis or cancer)

How to take TENOXICAM:

- Take TENOXICAM as directed by your doctor. Ask your healthcare professional if you have any questions.
- Do not take more of it, do not take it more often or do not take it for a longer period of time than prescribed by your doctor.
- Take this medicine immediately after a meal or with food to lessen the chance of stomach upset. If stomach upset (nausea, vomiting, stomach pain, diarrhea, or indigestion) occurs and persists, check with your doctor.
- You should take your dose at the same time each day.
- Check with your doctor if you are not getting relief or if any problems develop.

Usual dose:

Adults: The usual dose is 1 tablet (20 mg) each day.
Your healthcare professional may reduce your dose.

Overdose:

If you think you, or a person you are caring for, have taken too much TENOXICAM, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to take TENOXICAM, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose. Do not take two doses at the same time to make up for a missed dose.

What are possible side effects from using TENOXICAM?

These are not all the possible side effects you may have when taking TENOXICAM. If you experience any side effects not listed here, tell your healthcare professional.
Side effects include:

- nausea/vomiting
- indigestion/heartburn
- abdominal pain
- dry mouth
- constipation
- difficulty passing urine
- dizziness
- drowsiness
- tiredness
- sweating more than usual
- trouble sleeping

TENOXICAM can cause abnormal blood test results. Your healthcare professional will decide when to perform blood tests and interpret the results.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
COMMON			
Gastrointestinal (GI) bleeding (bleeding anywhere along the GI tract between mouth and anus): (bleeding in esophagus, stomach or first part of small intestines): blood in vomit, black tarry stool, bright red blood in your stool or coming from rectum, rapid pulse, low blood pressure, low urine flow, confusion, weakness, dizziness; (bleeding from large intestine, rectum): bright red blood in your stool or coming from rectum, rapid pulse, low blood pressure, low urine flow, confusion, weakness, dizziness			√
Nervous system problems: generally feeling unwell, tingling or numbness of the hands or feet, nervousness	√		
UNCOMMON			
Allergic reaction: skin rash, hives, itching, swelling of the face, lips, tongue or throat which may cause difficulty in swallowing or breathing			√
Gastrointestinal perforation (a hole in the wall of your stomach or bowels): severe abdominal pain and tenderness, nausea, vomiting, chills or fever			√
Stomach or duodenum ulcer: pain and discomfort (indigestion) which is felt between the navel and the breastbone, vomiting blood,			√

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
bloody or black tarry stools			
Heart problems: fast or irregular heartbeat, high blood pressure		√	
Kidney problems: blood in the urine			√
UNKNOWN			
Mental health problems: confusion		√	
Photosensitivity: increased sensitivity of the skin to sun (such as redness, itching, swelling, blistering)	√		
Blood related problems: Decreased number of red blood cells: tiredness, headaches, being short of breath when exercising, dizziness and looking pale; Lack of white blood cells: frequent infections such as fever, severe chills, sore throat or mouth ulcers; Low blood platelet count: bleeding or bruising more easily than normal.			√
Respiratory problems: bronchospasm: shortness of breath, chest tightness, wheezing or coughing			√
Liver problems: yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite		√	
Eyes, Ears, Nose, Throat: Vision abnormal; buzzing, ringing or other persistent noise in the ears; deafness; bleeding		√	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
from the nose;			
RARE			
Severe Skin Reactions: fever, severe rash, swollen lymph glands, flu-like feeling, blisters and peeling skin that may start in and around the mouth, nose, eyes and genitals and spread to other areas of the body, swelling of face and/or legs, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feeling thirsty, urinating less often, less urine or dark urine			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at room temperature 15°C to 30°C.
Keep out of reach and sight of children.

If you want more information about TENOXICAM:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html). Find the Patient Medication Information on the manufacturer's website (http://www. aapharma.ca/en/), or by calling 1877-998-9097.

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