SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Noxicam 8 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One film-coated tablet contains 8 mg lornoxicam.

Excipient with known effect: 90 mg lactose monohydrate.
For the full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

Off-White to yellow, convex, round film-coated tablet, with deep break-line at one side and shallow break-line on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Short-term treatment of moderate pain such as pain after dental surgery..
- treatment of pain associated with acute lumbo-sciatica.
- Symptomatic treatment of pain and inflammation in osteoarthritis and rheumatoid arthritis.

4.2 Posology and method of administration

Posology

For all patients the appropriate dosing regimen should be based upon individual response to treatment. Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

Pain
8-16 mg lornoxicam daily divided into 2 or 3 doses. The maximum recommended daily dose is 16 mg.

Osteoarthritis and rheumatoid arthritis
The recommended initial dose is 12 mg lornoxicam daily divided into 2 or 3 doses. The maintenance dose should not exceed 16 mg lornoxicam daily.

Special patient groups

Pediatric population
Lornoxicam is not recommended for use in children and adolescents under the age of 18 due to a lack of data on safety and efficacy.

Elderly patients
No special dosage modification is required for elderly patients above age 65, except in those with renal

or hepatic impairment. Nevertheless, lornoxicam should be administered with caution as gastrointestinal adverse effects are less well tolerated in this group (see section 4.4).

Renal impairment
In patients with mild to moderate renal impairment, the maximum recommended daily dose is 12 mg divided in 2 or 3 doses (see section 4.4). Lornoxicam is contraindicated in patients with severe renal impairment (see section 4.3).

Hepatic impairment
In patients with moderate hepatic impairment, the maximum recommended daily dose is 12 mg divided in 2 or 3 doses (see section 4.4). Lornoxicam is contraindicated in patients with severe hepatic impairment (see section 4.3).

Method of administration

For oral use.
Noxicam 8 mg film-coated tablets should be taken with a sufficient quantity of liquid.

4.3 Contraindications

- Hypersensitivity to lornoxicam or to any of the excipients listed in section 6.1.
- Thrombocytopenia
- Hypersensitivity reactions (symptoms like asthma, rhinitis, angioedema or urticaria) to other non-steroidal anti-inflammatory drugs (NSAIDs) including acetylsalicylic acid
- Severe heart failure
- Gastrointestinal hemorrhage, cerebrovascular hemorrhage or other bleeding disorders
- History of gastrointestinal hemorrhage or perforation, associated with a prior use of NSAIDs
- Active peptic ulcer/hemorrhage or history of recurrent peptic ulcer/hemorrhage (two or more distinct episodes of established ulceration or bleeding)
- Severe hepatic impairment
- Severe renal impairment (serum creatinine >700 μmol/L)
- Third trimester of pregnancy (see section 4.6)

4.4 Special warnings and precautions for use

Lornoxicam reduces platelet aggregation and prolongs bleeding time. For this reason, caution should be exercised when treating patients with a bleeding diathesis.

Lornoxicam should only be used after a careful benefit-risk assessment in patients with:
- impaired renal function – lornoxicam must be used with caution in patients with mild (serum creatinine 150-300 μmol/L) to moderate (serum creatinine 300-700 μmol/L) renal impairment due to the dependence on renal prostaglandins to maintain renal blood flow (see section 4.2). Treatment with lornoxicam should be discontinued if renal function becomes compromised during treatment.
- Renal function must be monitored in the following patients:
  - patients awaiting major surgery;
  - patients with heart failure;
  - patients receiving concomitant treatment with diuretics or medicinal products with known or suspected renal toxicity (see section 4.5).
- In patients with bleeding disorders, close clinical and laboratory monitoring is recommended (e.g. PTT).
- Impaired liver function (e.g. liver cirrhosis): In patients with impaired liver function, clinical and laboratory monitoring should be considered given that accumulation of lornoxicam (increase in AUC) may occur following treatment with daily doses of 12-16 mg (see section

5.2). That being said, impaired liver function is not expected to affect the pharmacokinetics of lornoxicam compared to that in healthy individuals.

- Patients receiving long-term treatment (longer than 3 months) with NSAIDs should have their liver and kidney parameters checked regularly. In addition, regular hematology laboratory tests should be performed.
- Monitoring of renal and liver function is recommended for elderly patients over 65 years of age. Caution is advised in elderly patients post surgery.

Concomitant use of NSAIDs

Concomitant use of lornoxicam and NSAIDs (including selective cyclooxygenase-2 inhibitors) should be avoided (see section 4.5).

Minimizing side effects

Side effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2 as well as "Gastrointestinal bleeding, ulceration and perforation" and "Cardiovascular and cerebrovascular effects" below).

Gastrointestinal bleeding, ulceration and perforation

Gastrointestinal (GI) bleeding, ulceration, or perforation, which may be fatal, have been reported with all NSAIDs and may occur at any time during therapy, with or without prior warning signs or a history of serious gastrointestinal events.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. In these patients, the treatment should be commenced using the lowest available dose (see section 4.2). Combination therapy with gastroprotective agents (e.g. misoprostol or proton pump inhibitors) should be considered in these patients, and also in patients requiring concomitant low-dose acetylsalicylic acid or other medicinal products that may increase the gastrointestinal risk (see below and section 4.5). Close clinical monitoring is recommended.

Patients with a history of GI toxicity, particularly when elderly, should be instructed to report any unusual abdominal symptoms (especially GI bleeding), especially in the initial stages of treatment. Caution should be exercised in patients receiving concomitant medicinal products which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as acetylsalicylic acid (see section 4.5).

If GI bleeding or ulceration occur in patients receiving lornoxicam, the treatment should be discontinued.

Caution is advised when administering NSAIDs to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease) as their condition may worsen (see section 4.8).

Elderly patients

Elderly patients display an increased frequency of adverse reactions to NSAIDs, particularly gastrointestinal bleeding and perforation, which may be fatal (see section 4.3).

Cardiovascular and cerebrovascular effects

Appropriate monitoring and counseling are required in patients with hypertension and/or mild to moderate decompensated heart failure (past or current) as fluid retention and edema have been

reported in association with NSAID therapy.

Clinical studies and epidemiological data suggest that the use of some NSAIDs (particularly in high-dose and long-term treatment) may be associated with an increased risk of arterial thrombotic events (e.g. myocardial infarction or stroke). There is insufficient data available to be able to rule out this risk for lornoxicam.

Patients with refractory hypertension, decompensated heart failure, existing ischemic heart disease, peripheral artery disease and/or cerebrovascular disease should only be treated with lornoxicam after careful consideration. Similar considerations should also be made before commencing long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidemia, diabetes, nicotine use).

The concomitant use of NSAIDs and heparin during spinal or epidural anesthesia increases the risk of spinal/epidural hematoma (see section 4.5).

Skin disorders

Serious, sometimes fatal, skin reactions, including exfoliative dermatitis, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported very rarely in association with the use of NSAIDs (see section 4.8). The highest risk of said reactions is likely to be at the start of therapy, with the majority of these reactions occurring within the first month of treatment. Lornoxicam should be discontinued at the first appearance of a skin rash, mucosal lesions or other signs of hypersensitivity.

Respiratory disorders

Caution should be exercised when using NSAIDs in patients suffering from bronchial asthma or patients with a history of asthma, as NSAIDs have been reported to cause bronchospasm in these patients.

Systemic lupus and mixed connective tissue disease

Caution is advised in patients with systemic lupus erythematosus (SLE) or mixed connective tissue disease, as they may be at increased risk of aseptic meningitis.

Nephrotoxicity

Concomitant treatment with NSAIDs and tacrolimus may increase the risk of nephrotoxicity due to reduced renal synthesis of prostacyclin. Renal function should therefore be closely monitored in patients receiving such combination therapy (see section 4.5).

Abnormal laboratory results

As with most other NSAIDs, increases in serum transaminases, increases in serum bilirubin or other liver function tests, and increases in serum creatinine and blood urea nitrogen (BUN), as well as other abnormal laboratory results, have been occasionally reported. If such abnormalities become significant or persist, lornoxicam should be discontinued and relevant investigations should be carried out.

Lactose

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, congenital (absolute) lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Fertility

The use of lornoxicam, like any medicinal product known to inhibit cyclooxygenase/prostaglandin synthesis, may impair fertility and is therefore not recommended for use in women planning pregnancy. Discontinuation of lornoxicam should be considered in women who have difficulty conceiving or are undergoing fertility testing (see section 4.6).

Varicella

In isolated cases, varicella can lead to serious infectious skin and soft tissue complications. As of yet, NSAIDs' association with the exacerbation of said infections cannot be ruled out. It is therefore advisable to avoid using lornoxicam in varicella.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of lornoxicam and

- Cimetidine: resulted in increased plasma concentrations of lornoxicam, which could increase the risk of adverse reactions to lornoxicam (No interactions were demonstrated between lornoxicam and ranitidine or between lornoxicam and antacids);
- Anticoagulants: NSAIDs may increase the effects of anticoagulants such as warfarin (see section 4.4). Close monitoring of the INR is indicated;
- Phenprocoumon: reduced effect of treatment with phenprocoumon;
- Heparin: NSAIDs increase the risk of bleeding and spinal or epidural hematoma when used concomitantly with heparin in conjunction with spinal or epidural anesthesia (see section 4.4);
- ACE inhibitors: the antihypertensive effects of ACE inhibitors may be reduced;
- Diuretics: reduced diuretic and antihypertensive effect of loop diuretics, thiazide diuretics, and potassium-sparing diuretics (increased risk of hyperkalemia and nephrotoxicity);
- Beta-blockers: reduced antihypertensive efficacy;
- Angiotensin II receptor blockers: reduced antihypertensive efficacy;
- Digoxin: reduced renal clearance of digoxin, increasing the risk of digoxin toxicity;
- Corticosteroids: increased risk of gastrointestinal ulcers or hemorrhage (see section 4.4);
- Quinolone antibiotics (e.g. levofloxacin, ofloxacin): increased risk of seizures;
- Antiplatelet agents (e.g. clopidogrel): increased risk of hemorrhage (see section 4.4);
- Other NSAIDs: increased risk of gastrointestinal hemorrhage or ulceration;
- Methotrexate: increased serum levels of methotrexate. This may lead to increased toxicity. If concomitant therapy is necessary, careful monitoring is advised;
- Selective serotonin reuptake inhibitors (SSRIs): increased risk of hemorrhage (see section 4.4);
- Lithium: NSAIDs inhibit the renal clearance of lithium, causing the serum lithium levels to possibly increase above toxicity limits. For this reason, serum lithium levels should be monitored, particularly at the start of therapy, at dose adjustments or on discontinuation of therapy;
- Cyclosporine: increased serum levels of cyclosporine. The nephrotoxicity of cyclosporine may be increased due to effects mediated by renal prostaglandins. During concomitant therapy, renal function should be monitored accordingly;
- Sulfonylureas (e.g. glibenclamide): increased risk of hypoglycemia;
- Known inducers and inhibitors of CYP2C9 isoenzymes: lornoxicam (like other NSAIDs dependent on cytochrome P450 2C9 (CYP2C9 isoenzyme)) displays interactions with known inducers and inhibitors of CYP2C9 isoenzymes (see section 5.2, Biotransformation);
- Tacrolimus: increases the risk of nephrotoxicity due to the reduced synthesis of prostacyclin in the kidneys. When used together, renal function should be monitored (see section 4.4);
- Pemetrexed: NSAIDs may decrease renal pemetrexed clearance, thereby increasing renal and gastrointestinal toxicity and leading to myelosuppression.

Noxicam 8 mg film-coated tablets display a delayed lornoxicam absorption when given with food. Therefore, Noxicam 8 mg film-coated tablets should not be taken with food if rapid onset of action (pain relief) is required.

One meal can reduce absorption by about 20% and increase T_{max} (see section 5.2).

4.6 Fertility, pregnancy and breast-feeding

Pregnancy

Lornoxicam is contraindicated in the third trimester of pregnancy (see section 4.3) and should not be used during the first and second trimesters of pregnancy and during delivery, as there is no clinical data on treatment during pregnancy.

There is insufficient data regarding the use of lornoxicam in pregnant women. Experimental studies on animals have shown reproductive toxicity (see Section 5.3)

Inhibition of prostaglandin synthesis can affect pregnancy and/or embryo/fetal development. It is assumed that the risk increases with increasing dose and duration of treatment. Data from epidemiological studies indicate an increased risk of miscarriage and cardiac malformations after the use of a prostaglandin synthesis inhibitor during early pregnancy. It is assumed that the risk increases with increasing dose and duration of treatment. In animals, the use of a prostaglandin synthesis inhibitor was shown to lead to increased pre- and post-implantation losses and increased mortality of the embryo or fetus. Prostaglandin synthesis inhibitors should therefore not be used during the first and second trimesters of pregnancy unless absolutely necessary.

From the 20th week of gestation onwards, the use of lornoxicam may cause oligohydramnios secondary to fetal renal impairment. This can occur shortly after starting treatment and is usually reversible after treatment is discontinued. In addition, there were reports of fetal ductus arteriosus constriction occurring after treatment in the second trimester of pregnancy, although it was reversible upon discontinuation of treatment in most cases. For this reason, lornoxicam should not be given during the first and second trimesters of pregnancy unless absolutely necessary. If lornoxicam is used in a woman who is trying to conceive or is in the first and second trimesters of pregnancy, the dose should be kept as low as possible and the duration of treatment as short as possible. After several days' use of lornoxicam from the 20th week of gestation, prenatal monitoring should be considered for oligohydramnios and fetal ductus arteriosus constriction. Lornoxicam should be discontinued if oligohydramnios or ductal constriction is detected.

During the third trimester of pregnancy, prostaglandin synthesis inhibitors can lead to fetal cardiopulmonary toxicity (with premature closure/constriction of the ductus arteriosus and pulmonary hypertension) and cause renal dysfunction (see above), which can progress to renal failure with oligohydramnios. In the mother and newborn, a possible prolongation of bleeding time may occur at the end of pregnancy, as well as inhibition of uterine contractions, which may lead to a delayed or prolonged delivery. The use of lornoxicam is therefore contraindicated during the third trimester of pregnancy (see section 4.3).

Breast-feeding

There is no data on the passage of lornoxicam into human breast milk. In lactating rats, however, lornoxicam passes into breast milk in relatively high concentrations. Lornoxicam should not be used in women who are breastfeeding.

Fertility

As with all active substances that inhibit cyclooxygenase/prostaglandin synthesis, the use of

lornoxicam can impair fertility and is therefore not recommended for women planning pregnancy. Discontinuation of lornoxicam should be considered in women who have difficulty conceiving or are undergoing fertility tests.

4.7 Effects on ability to drive and use machines

Patients who experience dizziness and/or drowsiness during treatment with lornoxicam should not drive or use machines.

4.8 Undesirable effects

Gastrointestinal toxicity is the most common side effect caused by NSAIDs. Peptic ulcers, perforations or gastrointestinal bleeding, which may sometimes be fatal, especially in the elderly (see section 4.4), nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, melena, hematemesis, ulcerative stomatitis, exacerbations of colitis and Crohn's disease (see section 4.4) have been reported following the use of NSAIDs. Gastritis was observed less frequently.

Approximately 20% of all patients treated with lornoxicam are expected to experience side effects. Among the most common side effects of lornoxicam are nausea, dyspepsia, indigestion, abdominal pain, vomiting and diarrhea. In the available studies, these symptoms generally occurred in less than 10% of patients.

Edema, hypertension and heart failure have been reported in association with NSAID treatment.

Clinical trials and epidemiological data suggest that the use of some NSAIDs (particularly in high-dose and long-term therapy) may be associated with a small increase in the risk of arterial thrombotic events (e.g. myocardial infarction or stroke) (see section 4.4).

In isolated cases, serious infectious skin and soft tissue complications may occur with varicella.

Table 1 below lists the side effects that primarily occurred in more than 0.05% of 6,417 patients in phase II, III and IV clinical trials.

The following convention is used to classify the frequencies of adverse reactions: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (frequency cannot be estimated from the available data).

Table 1: undesirable effects

System Organ Class	**Frequency Category**	**Adverse Reaction (Preferred Term)**
Infections and infestations	Rare	Pharyngitis
Blood and lymphatic system disorders	Rare	Anemia, thrombocytopenia, leukopenia, prolonged bleeding time
	Very rare	Ecchymosis. NSAIDs have been reported to cause potentially serious hematologic disorders as class effects, such as neutropenia, agranulocytosis, aplastic anemia, and hemolytic anemia.

Immune system disorders	Rare	Hypersensitivity including anaphylactoid reactions and anaphylaxis
Metabolism and nutrition disorders	Uncommon	Anorexia, weight changes
Psychiatric disorders	Uncommon	Insomnia, depression
	Rare	Confusion, nervousness, agitation
Nervous system disorders	Common	Mild and transient headache, dizziness
	Rare	Somnolence, paresthesia, dysgeusia, tremor, migraine
	Very rare	Aseptic meningitis in patients with SLE and mixed connective tissue disease (see section 4.4)
Eye disorders	Uncommon	Conjunctivitis
	Rare	Vision disorders
Ear and labyrinth disorders	Uncommon	Vertigo, tinnitus
Cardiac disorders	Uncommon	Palpitations, tachycardia, edema, heart failure (see section 4.4)
Vascular disorders	Uncommon	Flushing, edema
	Rare	Hypertension, hot flashes, bleeding, hematoma
Respiratory, thoracic and mediastinal disorders	Uncommon	Rhinitis
	Rare	Dyspnea, cough, bronchospasm
Gastrointestinal disorders	Common	Nausea, abdominal pain, dyspepsia, diarrhea, vomiting
	Uncommon	Constipation, flatulence, belching, dry mouth, gastritis, gastric ulcer, upper abdominal pain, duodenal ulcer, oral ulcers
	Rare	Melena, hematemesis, stomatitis, esophagitis, reflux, dysphagia, aphthous stomatitis, glossitis, perforated peptic ulcer, gastrointestinal bleeding
Hepatobiliary disorders	Uncommon	Elevated LFTs – SGPT (ALT) or SGOT (AST)

	Very rare	Hepatotoxicity, which leads to liver failure, hepatitis, jaundice and cholestasis
Skin and subcutaneous tissue disorders	Uncommon	Rash, pruritus, hyperhidrosis, erythematous rash, urticaria, angioedema, alopecia
	Rare	Dermatitis, eczema, purpura
	Very rare	Edema and bullous reactions, Stevens-Johnson syndrome, toxic epidermal necrolysis
Musculoskeletal and connective tissue disorders	Uncommon	Arthralgia
	Rare	Bone pain, muscle cramps, myalgia
Renal and urinary disorders	Rare	Nocturia, micturition disorders, elevated BUN and creatinine
	Very rare	Lornoxicam may trigger acute renal failure in patients with pre-existing renal impairment who are dependent on renal prostaglandins for maintenance of renal blood flow (see section 4.4). Various forms of nephrotoxicity including nephritis and nephrotic syndrome have been associated with NSAIDs as a class effect.
General disorders and administration site conditions	Uncommon	Malaise, facial edema
	Rare	Asthenia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

4.9 Overdose

There is currently no experience with acute overdose of lornoxicam to describe the consequences of an overdose or to recommend specific measures. However, the following symptoms can be expected after an overdose with lornoxicam: nausea and vomiting, cerebral symptoms (dizziness, visual disturbances). Serious symptoms such as ataxia (including coma and convulsions), liver and kidney damage and possibly coagulation disorders can also occur.

In the event of an actual or suspected overdose, the medicinal product should be discontinued. Due to

its short half-life, lornoxicam is rapidly excreted. Lornoxicam is not dialyzable. A specific antidote is currently not known. Usual emergency measures are indicated for treatment of overdose. In principle, the administration of activated charcoal can only reduce the absorption of the active substance immediately after lornoxicam is taken.
Gastrointestinal symptoms can be managed using prostaglandin analogues or ranitidine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Nonsteroidal anti-inflammatory and antirheumatic drugs, oxicams ATC code: M01AC05.

Mechanism of action

Lornoxicam is a non-steroidal anti-inflammatory drug with analgesic properties and belongs to the class of oxicams. Lornoxicam's mode of action is mainly based on the inhibition of the prostaglandin synthesis (inhibition of the cyclooxygenase enzyme). Inhibition of the cyclooxygenase enzyme leads to desensitization of peripheral nociceptors and, in turn, inhibition of inflammation. A central effect on nociception, which seems to be independent of anti-inflammatory effects, has also been suggested.

Pharmacodynamic effects

Lornoxicam has no effect on vital signs (e.g. body temperature, respiratory rate, heart rate, blood pressure, ECG, spirometry).

Clinical efficacy and safety

The analgesic properties of lornoxicam have been successfully demonstrated in several clinical trials during development of the drug.

Due to a local gastrointestinal irritation and a systemic ulcerogenic effect related to the inhibition of prostaglandin synthesis, gastrointestinal sequelae are common side effects after treatment with lornoxicam, as seen with other NSAIDs.

5.2 Pharmacokinetic properties

Absorption

Lornoxicam is rapidly and nearly completely absorbed from the gastrointestinal tract. Maximum plasma concentrations are achieved after approximately 1-2 hours. The absolute bioavailability of lornoxicam is 90-100%. A first-pass effect was not observed.

Taking Lornoxicam with meals reduces C_{max} by approximately 30%, while T_{max} increases from 1.5 to 2.3 hours. The absorption of lornoxicam (calculated using the AUC) can be reduced by up to 20%.

Distribution

Lornoxicam is found in the plasma in unchanged form and as its hydroxylated metabolite. The plasma protein binding of lornoxicam is 99% and is not concentration-dependent. After repeated intake it can also be detected in synovial fluid.

Biotransformation

Lornoxicam is extensively metabolised in the liver, primarily to the inactive 5–hydroxylornoxicam by hydroxylation. CYP2C9 is involved in the biotransformation of lornoxicam. Due to genetic polymorphism, slow and fast metabolizers exist for this enzyme, which may result in markedly increased plasma levels of lornoxicam in slow metabolizers. The hydroxylated metabolite does not display any pharmacological activity. Lornoxicam is metabolised completely. Approximately 2/3 is eliminated via the liver and 1/3 via the kidneys as an inactive substance.

When tested in animal models, lornoxicam did not induce liver enzymes. Clinical trial data do not reveal any evidence of accumulation of lornoxicam after repeated administration at recommended dosages. This finding was supported by post-marketing surveillance data from one-year studies.

Elimination

The mean elimination half-life of the parent compound is 3 to 4 hours. After oral administration, about 50% is excreted in the feces and 42% via the kidneys, mainly as 5-hydroxylornoxicam. After parenteral administration once or twice a day, the elimination half-life of 5-hydroxylornoxicam is about 9 hours. There is no evidence that the elimination rate changes with repeated intake.

In elderly patients above age 65, the clearance is reduced by 30-40%. Apart from the reduced clearance, there is no significant change in the kinetic profile of lornoxicam in elderly patients.

There is no significant change in the kinetic profile of lornoxicam in patients with impaired kidney or liver function, except for accumulation in patients with chronic liver disease after 7 days of treatment with daily doses of 12 and 16 mg.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeat-dose toxicity, reproductive toxicity, genotoxicity, and carcinogenic potential.

In single- and repeat-dose toxicity studies, lornoxicam caused renal toxicity and gastrointestinal ulcers in several species.

In rats, lornoxicam impaired fertility (effects on ovulation and implantation), and affected the pregnancy and delivery. In rabbits and rats, lornoxicam caused premature closure of the ductus arteriosus due to inhibition of cyclooxygenase.

In animals, the use of a prostaglandin synthesis inhibitor was shown to lead to increased pre- and post-implantation losses and increased mortality of the embryo or fetus. In addition, increased incidences of various malformations, including cardiovascular malformations, have been reported in animals receiving a prostaglandin synthesis inhibitor during organogenesis.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Lactose monohydrate
Microcrystalline cellulose (MCC) PH 101
Croscarmellose sodium
Povidone K-25
Magnesium stearate
Coating:

Ready to use coating blend (Hypromellose 2910, Titanium Dioxide, Macrogol 6000)
Iron yellow oxide
Macrogol 6000 (PEG)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

No special storage conditions

6.5 Nature and contents of container

PVDC/aluminum blister.

Pack sizes approved: 2, 7, 14, 10, 20 and 30film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORIZATION HOLDER

CTS CHEMICAL INDUSTRIES LTD, ISRAEL
3 HAKIDMA ST., KIRYAT MALACHI 83057, ISRAEL

8. MARKETINGAUTHORIZATION NUMBER(S)

178-04-36865-99

9. DATE OF REVISION OF THE TEXT

Revised in 05/2025 according to the MOH guidelines.