1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

LORNBLOC 4 mg film-coated tablets

LORNBLOC 8 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet of LORNBLOC 4 mg contains 4 mg lornoxicam.

Each film-coated tablet of LORNBLOC 8 mg contains 8 mg lornoxicam.

Each LORNBLOC 4 mg film-coated tablet contains 90 mg lactose monohydrate.

Each LORNBLOC 8 mg film-coated tablet contains 90 mg lactose monohydrate.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

LORNBLOC 4 mg is a white to yellowish, oblong film-coated tablet, debossed with "E04" on one side and plain on the other side.

LORNBLOC 8 mg is a white to yellowish, oblong film-coated tablet, debossed with "E05" on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- Short term treatment of mild to moderate pain associated with extra articular inflammation.
- 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.

Use the lowest effective dose for the shortest possible duration of treatment.

Adults (> 18 years of age)

Treatment of pain

8 mg to 16 mg per day given in 2 to 3 divided doses. The total daily dose should not exceed 16 mg.

Rheumatoid Arthritis (RA) and Osteoarthritis (OA)

Initial recommended total daily dose is 12 mg, divided in two or three doses. Maintenance dose should not exceed 16 mg per day.

Special populations

Elderly population

No special dosage modification is required for elderly patients (> 65 years), unless renal or hepatic function is impaired, in which case the daily dosage should be restricted (see section 4.4).

Renal impairment and hepatic impairment

For patients with renal or hepatic impairment the maximal recommended daily dose is reduced to 12 mg (one film-coated tablet LORNBLOC 4 mg three times per day). For details see section 4.4.

Paediatric population

LORNBLOC is not recommended for use in children under 18 years (see section 4.3).

Method of administration

LORNBLOC film-coated tablets are supplied for oral administration and should be taken before meals with a sufficient quantity of liquid.

4.3. Contraindications

LORNBLOC is contraindicated in:

- Patients with hypersensitivity to lornoxicam or to any excipients in LORNBLOC (see section 6.1).
- Patients who have suffered hypersensitivity reactions (bronchospasm, rhinitis, angioedema or urticaria) to other non-steroidal anti-inflammatory drugs (NSAIDs), including, acetylsalicylic acid.
- Patients with a history of gastrointestinal bleeding or perforation related to previous NSAID use.
- Patients who suffer from cerebrovascular bleeding.
- Patients with bleeding and coagulation disorders.

- Patient with active peptic ulcer or history of recurrent peptic ulceration/ haemorrhage/ perforations.
- Patient with severe liver impairment.
- Patient with severe renal impairment (serum creatinine > 700 µmol/L).
- Patients with thrombocytopenia.
- Patients who have heart failure.
- The elderly (> 65 years), those weighing less than 50 kg and those undergoing acute surgery.
- Patient under 18 years of age (see section 4.2).
- In pregnancy and lactation.

4.4. Special warnings and precautions for use

Hypersensitivity

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. LORNBLOC should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Drug reaction with eosinophilia and systemic symptoms

Drug reaction with eosinophilia and systemic symptoms (DRESS) has been reported in patients using NSAIDs such as LORNBLOC. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. 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. If such signs or symptoms are present, discontinue LORNBLOC and evaluate the patient immediately.

Gastrointestinal (GI) ulceration and bleeding in medical history

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events. The risk of gastrointestinal bleeding or perforation is higher with increasing doses of LORNBLOC in patients with a history of ulcers, particularly if complicated with haemorrhage or perforation (see section 4.3), and the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective medicines (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose acetylsalicylic acid or other active substances likely to increase gastrointestinal risk (see below and section 4.5). Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised 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 medicines such as acetylsalicylic acid (see section 4.5).

Clinical monitoring at regular intervals is recommended. Patients developing peptic ulceration and/or gastro- intestinal bleeding while taking LORNBLOC should discontinue medicine administration with appropriate therapeutic actions being taken.

LORNBLOC should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia) as the condition may be exacerbated.

LORNBLOC should only be administered after careful risk-benefit assessment in previous cerebrovascular haemorrhage, SLE, porphyria, haematopoietic disorders, patients with reduced cardiac function. When treating patients with mild to moderate cardiac failure, attention must be paid to the risk of fluid retention and decreased renal function.

Caution is required in patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with LORNBLOC therapy.

Studies and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). There are insufficient data to exclude such a risk for lornoxicam, as contained in LORNBLOC.
Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with LORNBLOC after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).
Hepatic impairment (e.g. liver cirrhosis)
Clinical monitoring and laboratory assessment at regular intervals is recommended (e.g. liver enzymes) as accumulation of lornoxicam, as contained in LORNBLOC (increase in AUC) may occur after treatment with daily doses of 12 to 16 mg. Apart from that, hepatic

impairment does not seem to affect pharmacokinetic parameters of lornoxicam as compared to healthy subjects (see section 4.3).

Renal impairment

Patients with mild renal impairment (serum creatinine 150 to 300 µmol/L) should be monitored quarterly, patients with moderate renal impairment (serum creatinine 300 to 700 µmol/L) should be monitored at 1 to 2-month intervals due to dependency on renal prostaglandins for maintenance of renal blood flow. Should renal function deteriorate during treatment, LORNBLOC should be discontinued (see section 4.3).

It is important to monitor renal function in patients:

- who are to undergo major surgery;
- with compromised renal function e.g. as a result of significant blood loss or severe dehydration;
- with cardiac failure;
- receiving concomitant treatment with diuretics;
- receiving concomitant treatment with medicines that are nephrotoxic.

Patients with coagulation disorders

Lornoxicam, as contained in LORNBLOC reduces platelet aggregation and prolongs bleeding time and consequently care should be taken when administering to patients with increased bleeding tendency. Patients with blood coagulation disorders, careful clinical monitoring and laboratory assessment is recommended (e.g. PTT).

Systemic lupus erythematosus (SLE)

In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis.

Asthma

Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients.

Long term treatment (longer than 3 months)

Regular laboratory assessments of haematology (haemoglobin), renal functions (creatinine) and liver enzymes is recommended.

Elderly patients (65 years or above)

The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation which may be fatal. There is no clinical experience with this dosage form in this patient group. Monitoring of renal and hepatic function is recommended. Precaution is advised in elderly postoperative patients.

NSAIDs

The use of lornoxicam, as contained in LORNBLOC with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided. Undesirable effects may be minimised by using lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and GI and cardiovascular risks above).

Heparin

Concomitant treatment with NSAIDs and heparin in the context of a spinal or epidural anaesthesia increases the risk of spinal/epidural haematoma (see section 4.5).

Tacrolimus

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

As with most NSAIDs occasional increase in serum transaminases level, increase in serum bilirubin or other liver function parameters, as well as increases in serum creatinine and blood urea nitrogen as well as other laboratory abnormalities have been reported. Should any such abnormality prove significant or persist, the administration of lornoxicam should be stopped and appropriate investigations prescribed.

Infections

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissues infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of lornoxicam in case of varicella.

Excipients

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take this medicine.

4.5. Interaction with other medicines and other forms of interaction

Known inducers and inhibitors of CYP2C9 isoenzymes lornoxicam, as contained in LORNBLOC has interactions with known inducers and inhibitors of CYP2C9 isoenzymes such as phenytoin, amiodarone, miconazole, tranylcypromine and rifampicin (see section 5.2).

Anticoagulants or platelet aggregation:

Concomitant administration of LORNBLOC and anticoagulants or platelet aggregation inhibitors may prolong the bleeding time. LORNBLOC may enhance the effects of anti-coagulants such as warfarin (see section 4.4). Careful monitoring of INR should be undertaken.

Methotrexate:

Increased serum concentration of high dose methotrexate; avoid concomitant use.
Special care must be taken if both NSAIDs and methotrexate are administered within 24 hours.

Lithium:

Might lead to an increase of the lithium peak concentration above toxicity limits and thus to a possible increase in adverse events. Therefore, serum lithium levels require monitoring,

especially during initiation, adjustment and withdrawal of treatment. Avoid concomitant use if frequent analysis of lithium concentration in plasma cannot be performed.

Sulphonylureas (e.g. glibenclamide):

May increase the hypoglycaemic effect.

Other NSAIDs and aspirin:

Increased risk of adverse reactions and increase the risk of gastrointestinal bleeding (see section 4.4).

Diuretics:

Decreased efficacy of loop diuretic medicines, thiazide diuretics, and potassium sparing diuretics. NSAIDs counteract the diuretic effect of furosemide.

ACE inhibitors:

The effect of the ACE inhibitor may decrease and there is a risk of acute renal insufficiency.

Cimetidine:

Higher plasma concentrations of lornoxicam. No interaction between lornoxicam and ranitidine, or lornoxicam and antacids has been demonstrated (see section 5.2).

Digoxin:

Decreased renal clearance of digoxin.

Ciclosporin:

Increased renal toxicity (nephrotoxicity) of ciclosporin may be enhanced via renal prostaglandin mediated effects. During combined treatment renal function should be monitored.

Corticosteroids:

Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

Antiplatelet medicines and selective serotonin reuptake inhibitors (SSRIs):

Increased risk of gastrointestinal bleeding (see section 4.4).

Heparin:

NSAIDs increase the risk of spinal or epidural haematoma when given concomitantly to heparin in the context of spinal or epidural anaesthesia (see section 4.4).

Beta-adrenergic blockers:

Decreased antihypertensive efficacy.

Angiotensin II receptor blocker:

Decreased antihypertensive efficacy.

Quinolone antibiotics:

Increased risk of seizures.

Tacrolimus:

Increase the risk of nephrotoxicity owing to reduced synthesis of prostacyclin in the kidney. During combined treatment renal function should be monitored (see section 4.4).

Pemetrexed:

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

4.6. Fertility, pregnancy and lactation

The use of LORNBLOC is contraindicated in pregnancy and lactation (see section 4.3).

Pregnancy

First trimester

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies raise concern about 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 %. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

Second and Third trimester.

During the third trimester of pregnancy, prostaglandin synthesis inhibitors, may expose the foetus to: cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension); renal dysfunction, which may progress to renal failure with oligo-

hydroamniosis. At the end of pregnancy, the mother and the neonate may be exposed 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 labour.

Breastfeeding

There are no data on the excretion of lornoxicam in human breast milk. Lornoxicam, as contained in LORNBLOC, is excreted in milk of lactating rats in relatively high concentrations. Therefore lornoxicam should not be used in breastfeeding women.

Fertility

The use of lornoxicam, as with any medicine 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 infertility, withdrawal of lornoxicam should be considered.

4.7. Effects on ability to drive and use machines

Adverse reactions such as dizziness or sleepiness have been reported in patients receiving LORNBLOC, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that LORNBLOC does not adversely affect their ability to do so (see section 4.8).

4.8. Undesirable effects

a) Summary of the safety profile

The most commonly observed adverse events of NSAIDs are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and

Crohn's disease (see section 4.4) have been reported following administration of NSAIDs. Less frequently, gastritis has been observed. Approximately 20 % of patients treated with lornoxicam can be expected to experience adverse reactions. The most frequent adverse effects of lornoxicam include nausea, dyspepsia, indigestion, abdominal pain, vomiting, and diarrhoea. These symptoms have generally occurred in less than 10% of patients in available studies. Oedema, hypertension, and cardiac failure have been reported in association with NSAID treatment.

Studies and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with an increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

Exceptionally, occurrence of serious cutaneous and soft tissues infectious complications during varicella.

b) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Infections and infestations		Pharyngitis	
Blood and the lymphatic system disorders		Anaemia, thrombocytopenia, leucopoenia, prolonged bleeding time, ecchymosis	
Immune system disorders		Hypersensitivity, anaphylactoid reaction and anaphylaxis	
Metabolism and nutrition disorders		Anorexia, weight changes	
Psychiatric disorders		Insomnia, depression, confusion, nervousness, agitation	
Nervous system disorders	Mild and transient headache, dizziness	Somnolence, paraesthesia, dysgeusia, tremor, migraine, aseptic	

		meningitis in patients with SLE and mixed connective tissue disorder (see section 4.4).	
Eye disorders		Conjunctivitis, visual disturbances	
Ear and labyrinth disorders		Vertigo, tinnitus	
Cardiac disorders		Palpitations, tachycardia, cardiac failure	
Vascular disorders		Flushing, oedema, hypertension, hot flush, haemorrhage, haematoma	
Respiratory, thoracic and mediastinal disorders		Rhinitis, dyspnoea, cough, bronchospasm	Symptoms of irritation in upper respiratory tract
Gastrointestinal disorders	Nausea, abdominal pain, dyspepsia, diarrhoea, vomiting	Constipation, flatulence, eructation, dry mouth, gastritis, gastric ulcer, abdominal pain upper, duodenal ulcer, mouth ulceration, stomatitis, oesophagitis, gastroesophageal reflux, dysphagia, aphthous stomatitis, glossitis, perforated peptic ulcer, gastrointestinal haemorrhage	Haemorrhoidal or rectal bleeding
Hepatobiliary disorders		Increase in liver function tests, SGPT (ALT) or SGOT (AST), hepatotoxicity resulting in e.g. hepatic failure, hepatitis, jaundice and cholestasis	
Skin and subcutaneous tissue disorders		Rash, pruritus, hyperhidrosis, rash erythematous, urticaria and angioedema, alopecia, dermatitis and eczema, purpura, oedema and bullous reactions, Stevens-Johnson syndrome, toxic epidermal necrolysis	Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) (see section 4.4).

Musculoskeletal and connective tissue disorders		Arthralgia, bone pain, muscle spasms, myalgia	Cramps in legs
Renal and urinary disorders		Nocturia, micturition disorders, increase in blood urea nitrogen and creatinine levels	
General disorders and administrative site conditions		Malaise, face oedema, asthenia	Debility, changes in appetite, increased sweating
Investigations			Increased transaminases

c) Description of selected adverse reactions

NSAIDs have been reported to cause potentially severe haematological disorders like neutropenia, agranulocytosis, aplastic anaemia, and haemolytic anaemia as class effects.

d) Other special populations

Renal impairment

Lornoxicam may precipitate 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). Nephrotoxicity in various forms including nephritis and nephrotic syndrome has been associated with NSAIDs as class effect.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to

SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9. Overdose

Symptoms

Overdose may cause nausea and vomiting, dizziness, ataxia, coma and cramps, liver and kidney damage, coagulation disorders.

Treatment

In the case of a real or suspected overdose, the medication should be withdrawn. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and class: A 3.1 Antirheumatics (anti-inflammatory agents)

Pharmacotherapeutic group: e.g. Anti-inflammatory and antirheumatic products, non-steroids

ATC code: M01AC05

Mechanism of action

Lornoxicam is a NSAID with analgesic properties and belongs to the class oxicams. The mode of action of lornoxicam is partly based on inhibition of prostaglandin synthesis (inhibition of the cyclo-oxygenase enzyme).

In vitro the inhibition of cyclo-oxygenase does not result in an increase in leukotriene formation. The mechanism of the analgesic action of lornoxicam has not been fully determined.

5.2. Pharmacokinetic properties

Absorption

Lornoxicam is absorbed rapidly and almost completely from the gastro-intestinal tract. Maximum plasma concentrations are achieved after approximately 1 to 2 hours. The absolute bioavailability (calculated on AUC) of lornoxicam is 90 to 100 %. No first-pass effect was observed. The mean elimination half-life is 3 to 4 hours. Simultaneous intake of lornoxicam with meals reduced C_{max} by approximately 30 %. T_{max} was increased from 1,5 to 2,3 hours. The absorption of lornoxicam (calculated on AUC) can be reduced by up to 20 %. Simultaneous intake with antacids has no effect on the pharmacokinetics of lornoxicam.

Distribution

Lornoxicam is found in the plasma in unchanged form and as its hydroxylated metabolite. The hydroxylated metabolite exhibits no pharmacological activity. The plasma protein binding of lornoxicam is 99 % and not concentration-dependent.

Biotransformation

Lornoxicam is metabolised completely, and approximately 2/3 is eliminated via the liver and 1/3 via the kidneys 2 as inactive substance. Lornoxicam is metabolized by cytochrome P450 2C9. Due to genetic polymorphism slow and rapid metabolisers exist for this medicine, which could result in markedly increased plasma levels of lornoxicam in slow metabolisers.

Elimination

In elderly subjects the clearance is reduced by 30 to 40 %. Apart from this reduced clearance there is no significant change in the kinetic profile of lornoxicam in elderly patients, or in patients with mild hepatic or kidney dysfunction.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Croscarmellose sodium, hypromellose (E464), lactose monohydrate, macrogol, magnesium stearate, microcrystalline cellulose, povidone, titanium dioxide (E171).

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at or below 30 °C.

6.5. Nature and contents of container

Clear polyvinylchloride/polyethylene/polyvinylidene chloride/aluminium blisters with 10 tablets per blister strip. 2 or 10 blister strips are packed into a carton in pack sizes of 20 or 100 tablets.

6.6. Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

LORNBLOC 4 mg: 48/3.1/0735

9. DATE OF FIRST AUTHORISATION

27 February 2024

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

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