SCHEDULING STATUS:

S1

1. NAME OF THE MEDICINE

LENAFEN, 200 mg, tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of LENAFEN contains:

Ibuprofen 200 mg

Contains sugar: Lactose monohydrate 274,625 mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablets.

White, film-coated biconvex tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

LENAFEN is indicated for the treatment of mild to moderate pain and fever of inflammatory origin for a treatment period not exceeding 10 days.

4.2 Posology and method of administration

Posology

Use the lowest effective dose for the shortest possible duration of treatment (see section 4.4).

Adults and children over 12 years:

Take 1 or 2 tablets every four to six hours after food or milk.

Do not exceed 6 tablets in any 24 hours.

Not to be given to children under 12 years.

LENAFEN should not be used continuously for fever for more than 3 days or for more than 10 days for pain without consulting a doctor.

Special populations

No information available.

Paediatric population

The safety and efficacy of LENAFEN in children under 12 years has not been established.

Method of administration

For oral administration.

4.3 Contraindications

- Patients with hypersensitivity to ibuprofen or to any of the excipients in LENAFEN (see section 6.1).
- LENAFEN should not be used in patients who have previously shown hypersensitivity reactions (e.g., asthma, urticaria, angioedema or rhinitis) after taking LENAFEN, aspirin or other NSAIDs.
- History of gastrointestinal perforation, ulceration and bleeding (PUB) related to previous NSAID therapy.
- Active or history of, recurrent peptic ulcer or haemorrhage or perforations.
- History of recurrent haemorrhage/perforations or in patients with conditions involving an increased tendency to bleeding e.g., haemophiliacs.
- Heart failure, severe hepatic impairment and severe renal impairment.
- Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/ foetal renal dysfunction and premature closure of the foetal

ductus arteriosus (see section 4.4 and 4.6).

4.4 Special warnings and precautions for use

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as LENAFEN. 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 LENAFEN and evaluate the patient immediately.

Severe hypokalaemia and renal tubular acidosis have been reported due to prolonged use of ibuprofen at higher than recommended doses. Ibuprofen induced renal tubular acidosis should be considered in patients with unexplained hypokalaemia and metabolic acidosis.

These have included reports of gastrointestinal perforations, gastrointestinal haemorrhages, severe anaemia, renal failure, renal tubular acidosis and severe hypokalaemia associated with the ibuprofen component.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms.

LENAFEN should be given with care to patients with asthma or bronchospasm, haemorrhagic disorders, a history of hypersensitivity to aspirin or NSAIDs, hypertension, impaired renal, hepatic, or cardiac function, peptic ulceration or a history of such ulceration, and in those

receiving warfarin. Patients undergoing therapy with some non-steroidal anti-inflammatories may need to be monitored for the development of blood, kidney, liver, or eye disorders.

Elderly

LENAFEN should be used with caution in the elderly. The elderly has an increased frequency of adverse reactions to NSAIDs such as LENAFEN, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.

The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing doses of LENAFEN, in patients with a history of ulcers (see section 4.3). These patients should commence treatment on the lowest dose available.

Gastrointestinal bleeding, ulceration and perforation

Gastrointestinal bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs including LENAFEN at any time during treatment, with or without warning symptoms or a previous history of serious gastrointestinal adverse events. Patients with a history of gastrointestinal disease, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding). Because of the adverse gastrointestinal effects, LENAFEN should be used with caution in patients with a history of peptic ulceration. Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, warfarin, selective serotonin-reuptake inhibitors or antiplatelet medicines such as aspirin, clopidogrel and ticlodipine (see Interactions with other medicines and other forms of interaction). When gastrointestinal bleeding or ulceration occurs in patients receiving LENAFEN, the treatment should be immediately withdrawn.

LENAFEN 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 these conditions may be exacerbated (see section 4.4 and section 4.8).

To reduce the risk of gastrointestinal effects, the medicine may be taken with or after food or milk. However, food and milk may reduce the rate and extent of the medicines absorption.

Cardiovascular and cerebrovascular effects

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

The use of LENAFEN, particularly at a high dose (2 400 mg/daily) and in long term treatment, may be associated with an increased risk of arterial thrombotic events such as myocardial infarction or stroke.

Patients with uncontrolled hypertension, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with LENAFEN after careful consideration.

Dermatological effects

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported (see section 4.4 and section 4.8). LENAFEN should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

As with other NSAIDs, LENAFEN should be used with caution in patients with infections, since symptoms such as fever and inflammation may be masked.

Caution should be used when initiating treatment with LENAFEN in patients with dehydration as renal failure may be precipitated. In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see below and Undesirable effects and Special warnings and precautions for use).

LENAFEN can interfere with platelet aggregation and has been shown to prolong bleeding

time in normal subjects. Patients who are sensitive to aspirin should not be given LENAFEN.

Excipients:

LENAFEN contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with the rare hereditary conditions of galactose intolerance e.g., galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption should not take LENAFEN.

Foetal Toxicity:

Limit use of NSAIDs, including LENAFEN, between 20 and 30 weeks of pregnancy due to the risk of oligohydramnios/foetal renal dysfunction. Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/foetal renal dysfunction and premature closure of the foetal ductus arteriosus (see section 4.6).

If NSAID treatment is necessary between 20 weeks and 30 weeks gestation, limit LENAFEN use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if LENAFEN treatment extends beyond 48 hours. Discontinue LENAFEN if oligohydramnios occurs and follow up according to clinical practice.

4.5 Interactions with other medicines and other forms of interaction

Care should be taken in patients treated with any of the following medicines as interactions have been reported.

Aminoglycosides: LENAFEN may decrease the excretion of aminoglycosides.

Anticoagulants: LENAFEN may enhance the effects of warfarin.

Antiplatelet medicines including aspirin, clopidogrel, ticlodipine and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding.

Antihypertensives, beta-blockers and diuretics: LENAFEN may reduce the effect of anti-hypertensives, such as ACE inhibitors, beta-blockers and diuretics. The risk of nephrotoxicity

may be increased with the use of ACE inhibitors or diuretics. There may also be an increased risk of hyperkalaemia with ACE inhibitors and potassium-sparing diuretics.

Aspirin: Concomitant administration of LENAFEN and aspirin is not recommended because of the potential of increased adverse effects.

Ciclosporin and tacrolimus: Increased risk of nephrotoxicity.

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding.

Digoxin: NSAIDs may exacerbate cardiac failure, reduced GFR and increase plasma cardiac glycoside levels. Digoxin blood levels should be monitored.

Cholestyramine: The concurrent administration of LENAFEN and cholestyramine reduces the absorption of LENAFEN in the gastrointestinal tract.

CYP2C9 Inhibitors: Concomitant administration of LENAFEN with CYP2C9 inhibitors may increase the exposure to ibuprofen (CYP2C9 substrate). In a study with voriconazole and fluconazole (CYP2C9 inhibitors), an increased S (+)-ibuprofen exposure by approximately 80 to 100 % has been shown.

Reduction of the LENAFEN dose should be considered when potent CYP2C9 inhibitors are administered concomitantly, particularly when high-dose LENAFEN is administered with either voriconazole or fluconazole.

Herbal extracts: Ginkgo biloba may potentiate the risk of bleeding with NSAIDs.

Lithium: Decreased elimination of lithium. Lithium levels should be monitored.

Methotrexate: NSAIDs may inhibit the tubular secretion of methotrexate, increase plasma concentrations and reduce clearance of methotrexate.

Mifepristone: A decrease in the efficacy of the medicinal product may occur due to the anti-prostaglandin properties of NSAIDs.

NSAIDs*:* Use of two or more NSAIDs concomitantly could result in an increase in side effects (see section 4.4).

Phenytoin: LENAFEN may enhance the effect of phenytoin.

Quinolone antibiotics: NSAIDs can increase the risk of convulsions associated with quinolone antibiotics.

Sulfonylureas: NSAIDs may potentiate the effects of sulfonylurea medications. There have been reports of hypoglycaemia in patients on sulfonylurea medications receiving LENAFEN.

Zidovudine*:* Increased risk of haematological toxicity when LENAFEN is given with zidovudine. There is evidence of an increased risk of hemarthrosis and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and LENAFEN.

LENAFEN can interfere with thyroid function tests by lowering serum thyroid hormone concentrations. In case of toxic effects, treatment with LENAFEN must be discontinued.

4.6 Fertility, pregnancy and lactation

Pregnancy

Use of NSAIDs, including LENAFEN, can cause premature closure of the foetal ductus arteriosus, persistent pulmonary hypertension of the new-born, foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, the use of LENAFEN dose and duration between 20 and 30 weeks of gestation should be limited and avoided at around 30 weeks of gestation and later in pregnancy. The onset of labour may be delayed and its duration increased (see section 4.4).

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after the use of a prostaglandin synthesis inhibitor such as LENAFEN in early pregnancy.

At the end of pregnancy, prostaglandin synthesis inhibitors may expose the mother and the neonate to the following:

- Prolongation of bleeding time.
- Inhibition of uterine contractions, which may result in delayed or prolonged labour.

Consequently, LENAFEN is contraindicated at 30 weeks and later of pregnancy.

Lactation

NSAIDs can appear in the breast milk in very low concentrations.

LENAFEN should not be used in breastfeeding mothers.

Fertility

The use of LENAFEN may impair female 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 LENAFEN should be considered.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

a. Summary of the safety profile

Adverse reactions are listed by system organ class.

b. Tabulated summary of adverse reactions

System organ class	Frequency	Undesirable effects
Infections and infestations	Less frequent	Rhinitis; Aseptic meningitis (especially in patients with existing autoimmune disorders, such as systemic lupus erythematosus and mixed connective tissue disease) with symptoms of stiff neck, headache, nausea, vomiting, fever or disorientation. (see section 4.4).
Blood and lymphatic system disorders	Less frequent	Leukopenia; Thrombocytopenia with or without

		purpura; Agranulocytosis; aplastic anaemia; haemolytic anaemia.
	Frequency Unknown	Neutropenia; inhibition of platelet aggregation is reversible
Immune system disorders	Less frequent	Hepatotoxicity and aseptic meningitis are hypersensitivity reactions that have been reported following treatment with NSAIDs.
	Frequency Unknown	Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of: (a) non-specific allergic reaction, anaphylaxis and fever (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses (including Stevens-Johnson

		syndrome, toxic epidermal necrolysis and erythema multiforme).
Psychiatric disorders	Less frequent	Confusional state; Nervousness and other central effects occur in some patients; Insomnia.
	Frequency Unknown	Anxiety; Depression; Hallucination.
Nervous system disorders	Frequent	Dizziness.
	Less frequent	Drowsiness
	Frequency unknown	Optic neuritis, headache, paraesthesia, somnolence.
Eye disorders	Frequency Unknown	Visual disturbances; Toxic optic neuropathy; Decreased visual acuity; Visual-field defects.
Ear and labyrinth disorders	Less frequent	Tinnitus.
	Frequency Unknown	Hearing impaired; Vertigo.
Cardiac disorders	Less frequent	Hypertension.
	Frequency Unknown	Oedema; Precipitation; Deterioration of cardiac failure.
Gastrointestinal disorders	Frequent	Nausea; Abdominal pain.

	Less frequent	Peptic ulcers; Perforation or gastrointestinal bleeding; Vomiting; Diarrhoea; Constipation; Melaena; Haematemesis (see section 4.4).
	Frequency unknown	Gastrointestinal perforation; Pancreatitis; Flatulence; Dyspepsia; Ulcerative stomatitis; Exacerbation of colitis and Crohn's disease; Gastritis (see also section 4.4)
Hepatobiliary disorders	Less frequent	Hepatitis; Jaundice.
	Frequency Unknown	Abnormal liver function; Hepatic failure.
Skin and subcutaneous tissue disorders	Frequent	Skin rash.
	Less frequent	Bullous reactions; Stevens-Johnson syndrome; Toxic epidermal necrolysis; Itching;

		Drug reaction with Eosinophilia and Systemic Symptoms (DRESS) (see section 4.4).
	Frequency unknown	Photosensitivity reaction.
Renal and urinary disorders	Less frequent	Impaired renal function.
	Frequency Unknown	Interstitial nephritis; Nephrotic syndrome; Acute renal failure; Chronic abuse of analgesics has been associated with nephropathy.
Metabolism and Nutrition Disorders	Unknown	Hypokalaemia*
Renal and urinary disorders	Unknown	Renal tubular acidosis*

Post marketing experience

No information available.

c. Description of selected adverse reactions

Gastrointestinal system disorders: The most commonly observed adverse events are gastrointestinal in nature.

Gastrointestinal bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs including LENAFEN Nausea and abdominal pain have been reported.

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. Health care providers

are requested to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. May also report to Adcock Ingram Limited using the following email: Adcock.AEReports@adcock.com

4.9 Overdose

Toxicity

Signs and symptoms of toxicity have generally not been observed at doses below 100 mg/kg in children or adults. However, supportive care may be needed in some cases.

Symptoms

Most patients who have ingested significant amounts of LENAFEN will manifest symptoms within 4 to 6 hours. The most frequently reported symptoms of overdose include epigastric pain, nausea, vomiting, abdominal pain, lethargy and drowsiness. Central nervous system (CNS) effects include headache, tinnitus, dizziness, convulsion, and loss of consciousness. Nystagmus, metabolic acidosis, hypothermia, renal effects, gastrointestinal bleeding, coma, apnoea, diarrhoea and depression of the CNS and respiratory system have also reported. Disorientation, excitation, fainting and cardiovascular been toxicity, including hypotension, bradycardia and tachycardia have been reported.

In cases of significant overdose, renal failure and liver damage may occur.

Prolonged use at higher than recommended doses may result in severe hypokalaemia and renal tubular acidosis. Symptoms may include reduced level of consciousness and generalised weakness (see section 4.4 and section 4.8).

Treatment

Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Electrolytes may be corrected by intravenous infusions, if necessary.

Dialysis may be done as LENAFEN is not strongly protein bound. There is no specific antidote to LENAFEN. Treatment is symptomatic and supportive. Good urine output should be

ensured.

Renal and liver function should be closely monitored. Patients should be observed for at least four hours after ingestion of potentially toxic amounts. Frequent or prolonged convulsions should be treated with intravenous diazepam. Other measures may be indicated by the patient's clinical condition.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 2.7 Antipyretic and anti-inflammatory analgesic

ATC code: M01AE01

Mechanism of action

Ibuprofen, a propionic acid derivative, is a non-steroidal compound, with analgesic, anti-inflammatory and antipyretic activities. Ibuprofen's therapeutic effect as an NSAID is thought to result from its inhibitory effect on the enzyme cyclo-oxygenase, which results in a marked reduction in prostaglandin synthesis. Ibuprofen is a cyclo-oxygenase inhibitor.

5.2 Pharmacokinetic properties

Absorption

Ibuprofen is rapidly absorbed from the gastrointestinal tract after oral administration, and peak plasma concentrations occur about 1 to 2 hours after ingestion.

Distribution

The elimination half-life in plasma is about 2 hours.

Metabolism

Ibuprofen is extensively (90 % to 99 %) bound to plasma proteins, but occupies only a fraction of the total drug-binding sites at usual concentrations. In experimental animals, ibuprofen and its metabolites pass easily across the placenta.

Elimination

The excretion of ibuprofen is rapid and complete. More than 90 % of an ingested dose is excreted in the urine as metabolites or their conjugates. The major metabolites are a hydroxylated and a carboxylated compound.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide;

Lactose monohydrate;

Magnesium stearate;

Povidone;

Polyethylene glycol;

Polyvinyl alcohol;

Purified talc;

Sodium starch glycollate;

Starch (maize);

Titanium dioxide (C.I. 77891) (E171).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from moisture.

Protect from light.

Keep blister in carton until required for use.

6.5 Nature and contents of container

12 or 24 tablets are packed in a clear polyvinylchloride blister strips sealed with an aluminium foil backing. The blister strips are packed into an outer cardboard carton together with a leaflet. Not all packs and pack sizes are necessarily marketed.

7. HOLDER OF CERTIFICATE OF REGISTRATION:

Adcock Ingram Limited

1 New Road,

Erand Gardens

Midrand,1685

Customer care: 0860ADCOCK/232625

8. REGISTRATION NUMBER(S)

L/2.7/354

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF AUTHORISATION

Date of Registration: 06 August 1979

10. DATE OF REVISION OF THE TEXT

Date of the most recent amendment to the professional information as approved by the Authority: 14 January 2026

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