PROFESSIONAL INFORMATION

SCHEDULING STATUS: S2

1. NAME OF THE MEDICINE

LOTEM SUSPENSION, 200 mg /250 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 ml contains:

Ibuprofen	200 mg
Paracetamol	250 mg

Preservatives:

Sodium benzoate	0,1 % *m/v*

Contains sodium metabisulphite as antioxidant

Contains sweeteners:

Saccharine sodium	12,40 mg
Sodium cyclamate	90,00 mg

Sugar free

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Suspension

A yellow, homogenous suspension with a banana odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

LOTEM SUSPENSION is indicated for fever and the relief of mild to moderate pain.

4.2 Posology and method of administration

Posology

Adults and children over twelve years: Take one to two medicine measures (5 to 10 ml) four hourly if necessary and not more than six medicine measures in twenty-four hours.

Children 2 to 5 years: 2.5 ml to 5 ml three to four times daily.

Children 6 to 12 years: 5ml to 10 ml three to four times daily.

Safety in children under two years of age has not been proven.

Consult your doctor if no relief is obtained with the recommended dosage.

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

Do not exceed the recommended dosage.

Shake the bottle before use.

Paediatric population

Safety in children under two years of age has not been proven.

Method of administration

LOTEM SUSPENSION should be taken orally, after meals with sufficient water.

4.3 Contraindications

- Impaired hepatic and renal function,
- Peptic ulceration or a history of such ulceration.
- Active or history of recurrent haemorrhage/perforations.
- History of gastrointestinal perforation, ulceration and bleeding (PUB) related to previous NSAID therapy.
- Heart failure.
- Hypersensitivity to any of the active ingredients, aspirin or other non-steroidal anti-inflammatory medicines, including any of the excipients listed in section 6.1. Because

of the possibility of cross-sensitivity due to the structural relationships which exist among non-steroidal anti-inflammatory medicines, acute allergic reactions may be more likely to occur in patients who have exhibited allergic reactions to these compounds.

- Do not use 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.
- Uncontrolled asthma or bronchospasm.
- Nasal polyps associated with aspirin-induced bronchospasm.
- Patients with bleeding disorders.
- Patients who are receiving coumarin-anticoagulants.

4.4 Special warnings and precautions for use

LOTEM SUSPENSION contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or Poison Centre must be contacted immediately.

The safety of continuous administration of LOTEM SUSPENSION has not been established for a period greater than four weeks.

Paracetamol:

Dosages in excess of those recommended may cause severe liver damage. Consult a doctor if no relief is obtained from the recommended dosage. Do not use for more than ten days without consulting a doctor. Use with caution in alcoholism or impaired liver function due to increased risk of hepatotoxicity.

Ibuprofen:

Ibuprofen should be given with care to the elderly, to patients with asthma or bronchospasm, bleeding disorders, cardiovascular disease or in liver or renal failure. Patients with congestive heart failure, cirrhosis, diuretic-induced volume depletion, or renal insufficiency require local synthesis of vasodilating prostaglandins to maintain renal perfusion and therefore, these patients are at greater risk of developing renal dysfunction due to NSAID-induced inhibition of renal prostaglandin synthesis.

Ibuprofen should be discontinued in patients who experience blurred or diminished vision or changes in colour vision.

Patients with collagen disease may be at increased risk of developing aseptic meningitis.

The antipyretic, analgesic and anti-inflammatory action of ibuprofen may mask symptoms of the occurrence or worsening of infection.

Diabetic patients: May experience false results with blood glucose tests.

Cardiovascular: 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 LOTEM SUSPENSION therapy. In view of the LOTEM SUSPENSION's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

Caution is required in patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) and should only be treated with diclofenac after careful consideration.

Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs including LOTEM SUSPENSION, 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 LOTEM SUSPENSION, in patients with a history of ulcers, and the elderly.

When gastrointestinal bleeding or ulceration occurs in patients receiving LOTEM SUSPENSION, treatment with LOTEM SUSPENSION should be stopped.

Gastrointestinal: LOTEM SUSPENSION should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, inflammatory or ulcerative disease of the upper or lower gastrointestinal tract, gastro-oesophageal reflux disease, angiodysplasia) as the condition may be exacerbated.

Skin reactions: Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. LOTEM SUSPENSION should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Foetal Toxicity: Limit use of NSAIDs, including LOTEM SUSPENSION, between 20 to 30 weeks of pregnancy due to the risk of oligohydramnios/foetal renal dysfunction.
If NSAID treatment is prescribed between 20 weeks and 30 weeks gestation, limit LOTEM SUSPENSION use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if LOTEM SUSPENSION treatment extends beyond 48 hours. Discontinue LOTEM SUSPENSION if oligohydramnios occurs and follow up according to clinical practice.

DRESS: Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as LOTEM SUSPENSION. 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. Eosinophillia 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 LOTEM SUSPENSION and evaluate the patient immediately.

LOTEM SUSPENSION should also be used with caution in the following conditions:

• Asthma - May be exacerbated.

• Allergic conditions - Possibility of cross sensitivity.

• Anaemia - May be exacerbated.

• Bleeding disorders - Increased risk of hepatotoxicity.

• Renal function impairment - Renal failure may be provoked, especially in patients with pre-existing renal impairment.

• Surgery: Possible enhanced bleeding if surgery is required.

4.5 Interaction with other medicines and other forms of interaction

• NSAIDs: use of two or more NSAIDs concomitantly could result in an increase in side effects.

• Corticosteroids: increased risk of gastrointestinal perforation, ulceration or bleeding (PUBs).

• Anti-coagulants: LOTEM SUSPENSION may enhance the effects of anti-coagulants such as warfarin.

• Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding.

• Hepatotoxic medicines: Increased risk of hepatotoxicity.

• Enzyme inducing medicines: Increased risk of hepatotoxicity. Possible decrease in therapeutic effects of paracetamol.

• Metoclopramide: Absorption of paracetamol may be accelerated.

• Cholestyramine: Absorption of paracetamol is reduced if given within one hour of cholestyramine.

• Alcohol, clopidogrel, ticlopidine, bisphosphonates, pentoxifylline: Increased risk of gastrointestinal bleeding and ulceration.

• Antidiabetic agents: Hypoglycaemic effects of these medicines may be increased.

• Digoxin: Increase in serum digoxin concentrations.

• Lithium: Increase in the steady-state concentration of lithium.

• Methotrexate: Increased and prolonged methotrexate plasma concentration and increased risk of methotrexate toxicity.

• Nephrotic medicines e.g., ciclosporin: Increased risk of nephrotoxicity.

• Antihypertensives or diuretics: Reduction or reversal of the antihypertensive effect may occur.

• Bone marrow depressants: The leucopenic and/or thrombocytopenic effects of these medicines may be increased.

4.6 Fertility, pregnancy, and lactation

LOTEM SUSPENSION is not recommended for use by pregnant or breastfeeding women.

Use of NSAIDs, including LOTEM SUSPENSION, can cause premature closure of the foetal ductus arteriosus and foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, the use of LOTEM SUSPENSION 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. If NSAIDs treatment is prescribed between 20 weeks and 30 weeks gestation, limit LOTEM SUSPENSION use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if LOTEM SUSPENSION treatment extends beyond 48 hours, (see section 4.3 “Contraindications” and section 4.4 “Warnings and special precautions for use”)

4.7 Effects on ability to drive and use of medicines

The effects on ability to drive and use machines has not been established.

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**
Blood and lymphatic system disorders	Less frequent	Anaemias, thrombocytopenia, neutropenia, eosinophilia and agranulocytosis. Leucopenia and pancytopenia. Fluid retention may occur.
Cardiac disorders	Less frequent	Tachycardia, flushing, increase in blood pressure/ hypertension, heart failure.
Immune system disorders	Less frequent	Hypersensitivity reactions fever, asthma and rashes. Other allergic reactions may be accompanied by fever and mucosal lesions. Hepatotoxicity and aseptic meningitis.
Nervous system disorders	Frequent	Dizziness.
	Less frequent	Headache, nervousness, tinnitus, depression, drowsiness and insomnia.
Eye disorders	Less frequent	Blurred vision, changes in colour perception and toxic amblyopia.
Gastrointestinal disorders	Frequent	Nausea, abdominal pain, vomiting, diarrhoea, flatulence, constipation, dyspepsia, peptic ulceration, perforation or gastrointestinal bleeding ,sometimes fatal, melena, haematemesis, gastritis.
	Less frequent	Pancreatitis, ulcerative stomatitis, exacerbation of colitis and Crohn’s disease.

Hepatobiliary disorders	Less frequent	Hepatitis.
Renal and urinary disorders	Less frequent	Oedema, impairment of renal function, acute reversible renal impairment.
	Frequency unknown	Nephrotoxicity interstitial nephritis, nephrotic syndrome and renal failure.
Skin and subcutaneous tissue disorders	Frequency unknown	Allergic dermatitis, erythema multiforme, bullous reactions including Stevens-Johnson syndrome, skin rashes, urticarial rash and toxic epidermal necrolysis. Drug reaction with eosinophilia and systemic symptoms (DRESS) (see **section 4.4**).

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 drug 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

Ibuprofen:

The most likely symptoms of overdosage are epigastric pain and nausea. Treatment is symptomatic and supportive.

Paracetamol:

Prompt treatment is essential: In the event of an overdosage, consult a doctor immediately, or take the person directly to a hospital. A delay in starting treatment may mean that antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed.

Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5 -10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of drugs that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Mild symptoms during the first two days of acute poisoning, do not reflect the potential seriousness of the overdosage.

Liver damage may become apparent 12 to 48 hours, or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and death.

Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac arrhythmias have been reported.

Treatment for paracetamol overdosage:

N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken. An initial dose of 150 mg/kg N-acetylcysteine in 200 ml dextrose injection given intravenously over 15 minutes, followed by an infusion of 50 mg/kg in 500 ml dextrose injection

over the next four hours, and then 100 mg/kg in 1 000 ml dextrose injection over the next sixteen hours. **The volume of intravenous fluid should be modified for children.**
Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by 70 mg/kg every four hours for seventeen doses.

A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdosage. Levels done before four hours may be misleading. Patients at risk of liver damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their 4-hour plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the nomogram below. The nomogram should be used only in relation to a single acute ingestion.
Those whose plasma paracetamol levels are above the “normal treatment line”, should continue N-acetylcysteine treatment with 100 mg/kg IV over sixteen hours repeatedly until recovery. Patients with increased susceptibility to liver damage as identified above, should continue treatment if concentrations are above the “high risk treatment line”. Prothrombin index correlates best with survival.

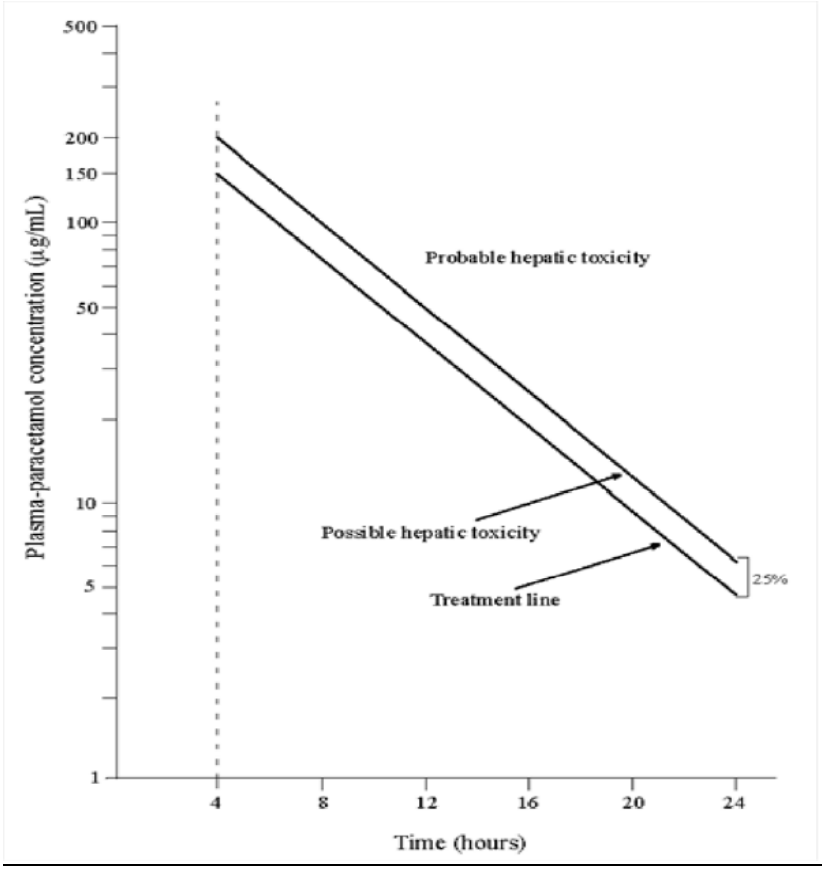


Figure 1. A semi-logarithmic plot of plasma-paracetamol concentration against hours after ingestion.

Monitor all patients with significant ingestions for at least ninety six hours.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 2.8 Analgesic combinations

Mechanism of action

LOTEM SUSPENSION has an analgesic, anti-inflammatory and antipyretic action.

5.2 Pharmacokinetic properties

Paracetamol:

Absorption following oral administration is well and almost complete. Paracetamol is metabolized in the liver primarily by conjugation. Paracetamol has a half-life of 1 to 4 hours, time to peak concentration of 0,5 to 2 hours, time to peak effect of 1 to 3 hours and the duration of action of 3 to 4 hours. Paracetamol is renally excreted primarily as metabolites and 3 % of a dose may be excreted unchanged.

Ibuprofen:

Well absorbed after oral administration. Onset of action for pain relief is 30 minutes and time to peak effect for fever is 2 to 4 hours. The half-life of ibuprofen is about 2 hours and the duration of action for fever is 6 to 8 hours or more and is 4 to 6 hours for pain. More than 90 % of an ingested dose is excreted in the urine as metabolite or their conjugates. Protein binding of ibuprofen is more than 95 %.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Banana flavour, citric acid anhydrous, colour spectracol quinoline yellow, disodium edetate, glycerol, light kaolin (low bioburden), polyethylene glycol, polyvinylpyrolidone k25, saccharin sodium, sodium citrate, sodium cyclamate, sodium dihydrogen phosphate dihydrate, sodium metabisulphite, sodium benzoate, xanthan gum.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

24 months.

6.4 Special precautions for storage

Store at or below 30 °C in well-closed containers.

Protect from light.

6.5 Nature and contents of container

Amber colour round glass bottles of 100 ml and 200 ml, with closure screw cap polypropylene lined with an expanded polyethylene liner.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand, 1685

Customer Care: 0860 ADCOCK /232625

8. REGISTRATION NUMBER

30/2.8/0391

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

07 November 1996

10. DATE OF REVISION OF THE TEXT

22 February 2024

Botswana: S3 BOT1502743

Namibia: NS1 04/2.8/1574