PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1 NAME OF MEDICINE

IBUNATE 200 mg TABLETS film-coated tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains: Ibuprofen 200 mg.

Contains sugar:

Lactose monohydrate 120, 0 mg per tablet.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets.

Pink, round, biconvex, film coated tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

IBUNATE 200 mg TABLETS is indicated for the treatment of:

- Rheumatoid arthritis.
- Idiopathic juvenile arthritis (Still’s disease).
- Ankylosing spondylitis.
- Osteoarthritis.
- Acute gouty arthritis.

- Non-articular rheumatism including fibrositis.
- Non-rheumatic inflammatory conditions such as frozen shoulder (capsulitis), bursitis, tendonitis, tenosynovitis and low back pain.
- Relief of mild to moderate pain such as dysmenorrhea, dental, post-episiotomy and post-partum pain.
- Soft tissue injuries such as sprains and strains.
- Pyrexia.

4.2 Posology and method of administration

Adults:

Acute: 1 200 mg to 2 400 mg per day in divided doses.

Maintenance: 600 mg to 1 200 mg per day in divided doses.

The total daily doses should not exceed 2 400 mg per day.

Method of administration

The tablets should be taken with food or milk to minimise gastro-intestinal side effects. If gastro-intestinal disturbance occurs, IBUNATE 200 MG TABLETS should be given with food or milk.

Paediatric population

This formulation is not suitable for children under the age of 12 years.

4.3 Contraindications

- Hypersensitivity to Ibuprofen or to any of the excipients listed in section 6.1.
- Use in Pregnancy and lactation is not recommended.
- Heart failure.

- Peptic ulcer disease or gastrointestinal bleeding.
- History of gastrointestinal bleeding or perforation (PUBs) related to previous NSAIDs.
- Acute or history of recurrent ulcer/haemorrhage/perforations.
- Patients sensitive to aspirin or another nonsteroidal anti-inflammatory medicine.
- History of severe allergic reaction such as anaphylaxis or angioedema, induced by aspirin or other NSAIDs. Because of the possibility of cross-sensitivity due to structural relationships which exists among non-steroidal anti-inflammatory medicines, acute allergic reactions are likely to occur in patients who have exhibited allergic reactions to these compounds.
- IBUNATE 200 mg TABLETS is contraindicated in patients with renal failure.
- Aspirin-induced nasal polyps associated with bronchospasm.
- Children under the age of 12 years.
- The use of IBUNATE 200 mg TABLETS around 20 weeks gestation or later in pregnancy may cause a rare but serious foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment (see section 4.4 and 4.6).
- Third trimester of pregnancy and during labour (see section 4.6).

4.4 Special warnings and precautions for use

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

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 IBUNATE 200 mg TABLETS. The risk of gastrointestinal bleeding or perforation (PUBs) is higher with increasing doses of with IBUNATE 200 mg TABLETS, in patients with a history of ulcers, and the elderly. When

gastrointestinal bleeding or ulceration occurs in patients receiving with IBUNATE 200 mg TABLETS, treatment with IBUNATE 200 mg TABLETS should be stopped with IBUNATE 200 mg TABLETS 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. Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. with IBUNATE 200 mg TABLETS should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Elderly: the elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation (PUBs) which may be fatal.

The use of IBUNATE 200 mg TABLETS around 20 weeks gestation or later in pregnancy may cause foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Complications of prolonged oligohydramnios include limb contractures and delayed lung maturation, which may require invasive procedures such as exchange transfusion of dialysis. If NSAID treatment is determined necessary, limit use to the lowest effective dose and shortest duration possible.

Regular use of NSAIDs during the third trimester of pregnancy may result in premature closure of the foetal ductus arteriosus in utero and possibly in persistent pulmonary hypertension of the new born. The onset of labour may be delayed and its duration increased.

Consider ultrasound monitoring of amniotic fluid if NSAID treatment extends beyond 48 hours. Discontinue the NSAID if oligohydramnios occurs (see section 4.3 and 4.6).

Risk benefit should be considered when the following medical conditions exist:

- IBUNATE 200 mg TABLETS should be given with care to the elderly, to patients with asthma or bronchospasm, cardiovascular disease, peptic ulceration, bleeding

disorders or a history of such ulceration, renal failure and in those receiving coumarin anticoagulants, liver or renal impairment.

- Patients with congestive cardiac 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 inhibition of renal prostaglandin synthesis.
- Because of the possibility of cross-sensitivity due to 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.
- Serious interactions have been reported after the use of high dose methotrexate with Ibuprofen.
- Patients receiving warfarin and other anti-coagulants. Patients who are sensitive to aspirin or other NSAIDs should generally not be given ibuprofen.
- IBUNATE 200 mg TABLETS should be discontinued in patients who experience blurred or diminished vision, or changes in colour vision.
- Patients with collagen disease may be at risk of developing aseptic meningitis.
- Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as IBUNATE 200 mg TABLETS. 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 IBUNATE 200 mg TABLETS and evaluate the patient immediately.

- Mild reactions such as allergic rhinitis, urticaria or skin rash induced by aspirin or other NSAIDs.
- Anaemia.
- Stomatitis.
- System lupus erythematosus.
- Renal Tubular Acidosis

Severe hypokalaemia and renal tubular acidosis have been reported due to prolonged use of NSAIDs at higher than recommended doses. Presenting signs and symptoms included generalised weakness. NSAID induced renal tubular acidosis should be considered in patients with unexplained hypokalaemia and metabolic acidosis.

Contains sugar (lactose monohydrate)

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

4.4 Interaction with other medicines and other forms of interaction

- Anti-hypertensives, beta-blockers and diuretics: IBUNATE 200 mg TABLETS may reduce the effect of anti-hypertensives, such as ACE inhibitors, beta-blockers and diuretics.
- Serious interactions have been reported after the use of high dose methotrexate with ibuprofen.
- NSAIDs: use of two or more NSAIDs concomitantly could result in an increase in side-effects.
- Corticosteroids: increased risk of gastrointestinal ulceration or bleeding (PUBs).

- Anti-coagulants: IBUNATE 200 mg TABLETS may enhance the effects of anti-coagulants such as warfarin.
- Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding.
- Diuretics can also increase the risk of nephrotoxicity of IBUNATE 200 mg TABLETS.
- Digoxin: Increase in serum digoxin concentrations. More frequent monitoring is mandatory and may exacerbate cardiac failure and reduce GFR.
- Lithium: Increase in the steady-state concentration of lithium. More frequent monitoring is mandatory.
- Immunosuppressive medicines e.g. ciclosporin: Increased risk of nephrotoxicity.
- Mifepristone: A decrease int eh efficacy of the medicinal product can theoretically occur due to the anti-prostaglandin properties of IBUNATE 200 mg TABLETS. Limited evidence suggests that coadministration of IBUNATE 200 mg TABLETS on the day of prostaglandin administration does not adversely influence the effects of mifepristone or the clinical efficacy of medicinal termination of pregnancy.
- Quinolone antibiotics: Patients taking IBUNATE 200 mg TABLETS and quinolones may have an increased risk of developing convulsions.
- Aminoglycosides: IBUNATE 200 mg TABLETS may decrease the excretion of aminoglycosides.
- Herbal extracts: Ginkgo biloba may potentiate the risk of bleeding with IBUNATE 200 mg TABLETS.
- Alcohol, corticosteroids, clopidogrel, ticlopidine, bisphosphonates, pentoxifylline – Increased risk of gastrointestinal bleeding and ulceration.
- Antidiabetic medicines: hypoglycaemic effects of these medicines may be increased.
- Methotrexate: Increase and prolonged methotrexate plasma concentration and an increased risk of methotrexate toxicity. More frequent monitoring is mandatory.

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

4.6 Fertility, pregnancy and lactation.

Use in Pregnancy and lactation is not recommended.

Regular use of non-steroidal inflammatory drugs may result in:

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.

The onset of labour may be delayed and its duration increased.

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.

Pregnant women should not use IBUNATE 200 mg TABLETS at 20 weeks or later unless specifically advised to do so by a health care professional because it may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment.

Additionally it should be avoided at 30 weeks and later in pregnancy because of the additional risk of premature closure of the fetal ductus arteriosus (see Section 4.3 and 4.4).

Breastfeeding

Safety and efficacy in lactation have not been established (see section 4.3)

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking IBUANTE 200 mg TABLETS. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

The frequency of adverse reactions reported are summarised in Table 1 as per the MedDRA system organ classification (SOC).

Table 1: Tabulated list of adverse reactions		
System Organ Class	**Frequency**	**Adverse effect**
Blood and lymphatic system disorders	Less frequent	Agranulocytosis, thrombocytopenia, anaemias, neutropenia, eosinophilia.

Immune system disorder	Less frequent	Aseptic meningitis, angioedema, anaphylaxis, fever, rashes, exacerbation of asthma and bronchospasm.
Metabolism and nutrition disorders	Frequency not known	Hypokalaemia.
Psychiatric disorders	Frequent	Depression.
Nervous system disorders	Frequent	Dizziness, nervousness, tinnitus, drowsiness, insomnia.
	Less frequent	Headache.
Eye disorders	Less frequent	Blurred vision.
	Frequency not known	Visual impairment, changes in visual colour perception and other toxic amblyopia.
Cardiac disorders	Less frequent	Tachycardia, flushing.
	Frequency not known	Increase in blood pressure/hypertension, oedema, cardiac failure.
Gastrointestinal disorders	Frequent	Nausea, abdominal cramps and pain. Vomiting, diarrhoea, flatulence, constipation, dyspepsia, peptic ulcers, perforation or gastro-intestinal bleeding (sometimes fatal), melaena, haematemesis, gastritis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease.
	Less frequent	Abdominal discomfort or pain, gastro-intestinal ulcers, sometimes with bleeding.
Hepato-biliary disorders	Less frequent	Hepatitis. Hepatotoxicity, abnormalities in liver function tests.

Skin and subcutaneous tissue disorders	Less frequent	Allergic dermatitis, erythema multiforme
	Frequency not known	Bullous reactions including Stevens Johnson syndrome and toxic epidermal necrolysis. Drug reaction with Eosinophilia and Systemic Symptoms (DRESS) (see section 4.4)
Renal and urinary disorders	Less frequent	Oedema, impairment of renal function, cystitis, haematuria, acute reversible renal impairment, interstitial nephritis and nephrotic syndrome.
	Frequency not known	Renal tubular acidosis.

Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting typically following prolonged use of higher than recommended doses.

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 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. Alternately please contact Gulf Drug Company (Pty) Ltd on +27 31 538 8700 or info@gulfdrug.co.za.

4.9 Overdose

The most likely symptoms are epigastric pain and nausea.

Electrolytes may be corrected by intravenous infusions if necessary.

There is no specific antidote for IBUNATE 200 mg TABLETS.

Treatment is symptomatic and supportive.

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 4.8).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 3.1 Antirheumatics (anti-inflammatory agents)

ATC code: M01A E01

Ibuprofen is a propionic acid derivative and has anti-inflammatory, analgesic and anti-pyretic properties.

5.2 Pharmacokinetic properties

Ibuprofen is absorbed following oral administration, and peak concentrations are observed after 1 to 2 hours. The half-life in plasma is about 2 hours. Ibuprofen is extensively bound to plasma-proteins. It is rapidly excreted in the urine, approximately 90% of the dose being recovered as metabolites and their conjugates. Ibuprofen passes slowly into the synovial spaces, remaining there in higher concentrations, as the plasma concentration of Ibuprofen declines.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Uncoated tablet:

- Lactose monohydrate
- Magnesium stearate

- Microcrystalline cellulose pH 102
- Pregelatinised starch

Coating:

- Opadry II Pink or Flexicoat Pink V6

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a cool dry place at or below 25°C. Protect from light.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

Patient ready packs of 15 and 84 tablets

Plastic Containers of 20, 30, 100, 500, 1000 tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Gulf Drug Company (Pty) Ltd

22 Burnside Drive

Old Mill Industrial Park

Mount Edgecombe, 4300

www.gulfdrug.co.za

8 REGISTRATION NUMBER

29/3.1/0727

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATION

OCTOBER 1994

10 DATE OF REVISION OF THE TEXT

01 March 2024

P/290727/5