SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

BETAPROFEN® 200 (TABLETS)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200 mg Ibuprofen

For full list of excipients, see section 6.1

Contains sugar: Sucrose: 84,3 mg per tablet and lactose: 102,74 mg per tablet

3. PHARMACEUTICAL FORM

Tablet.

Pink, round, biconvex, sugar-coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Osteoarthritis, rheumatoid arthritis and other musculoskeletal disorders.

4.2 Posology and Method of Administration

Posology

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 dose should not exceed 2 400 mg per day.

To minimize gastrointestinal side-effects or if gastrointestinal disturbances occur,

BETAPROFEN® should be given with food or milk.

4.3 Contraindications

BETAPROFEN® 200 should not be given to patients with:

- Peptic ulceration
- History of gastrointestinal perforation, ulceration or bleeding (PUB) related to previous NSAID's use.
- Active history of recurrent ulcer, haemorrhage or perforations.
- **BETAPROFEN® 200** is contraindicated in patients who are hypersensitive to ibuprofen, aspirin or any other non-steroidal anti-inflammatory agent. 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.
- **BETAPROFEN® 200** is contraindicated in patients with heart failure.
- **BETAPROFEN® 200** is contraindicated in patients with renal failure.
- The use of **BETAPROFEN® 200** 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

- **BETAPROFEN® 200** should be given with care to patients with asthma or bronchospasm, cardiovascular disease, peptic ulceration or a history of such ulceration, bleeding disorders, renal failure and to those receiving coumarin anticoagulants.
- 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 **BETAPROFEN® 200** therapy. In view of **BETAPROFEN® 200**'s inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.
- Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs including **BETAPROFEN® 200**, 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 **BETAPROFEN® 200**, in patients with a history of ulcers, and the elderly.
- When gastrointestinal bleeding or ulceration occurs in patients receiving **BETAPROFEN® 200**, treatment with **BETAPROFEN® 200** should be stopped.
- **BETAPROFEN® 200** 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, Steven Johnson Syndrome, and toxic epidermal necrolysis have been reported. **BETAPROFEN® 200** should be discontinued at the first appearance of skin rash, mucosal lesion, or any other sign of hypersensitivity.
- The use of **BETAPROFEN® 200** around 20 weeks gestation or later in pregnancy may cause fetal 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 or dialysis. If NSAID treatment is determined necessary, limit use to the lowest effective dose and shortest duration possible.

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.

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)**.**

- **BETAPROFEN® 200** contains lactose monohydrate and should not be given to patients with rare hereditary problems or a history of galactose intolerance, lapp lactase deficiency or glucose-galactose malabsorption.
- **BETAPROFEN® 200** should be given with care to the elderly, to patients with asthma or bronchospasm, bleeding disorders, cardiovascular disease, a history of peptic ulceration, and 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 prostaglandins synthesis.
- Because of the possibility of cross-sensitivity due to structural relationships which exists 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.
- Care is required in those who are also receiving warfarin and other anti-coagulants. Patients

who are sensitive to aspirin or other NSAIDs should generally not be given ibuprofen.

- 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.
- Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as **BETAPROFEN® 200.** 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 **BETAPROFEN® 200** and evaluate the patient immediately.
- **Renal:**

  Renal impairment as renal function may deteriorate (see sections 4.3 and 4.8). There is a risk of renal impairment in dehydrated children and adolescents.

  Severe hypokalaemia and renal tubular acidosis have been reported due to prolonged use of ibuprofen at higher than recommended doses. This risk is increased with the use of codeine/ibuprofen as patients may become dependent on the codeine component (see warning on Opioid use disorder, section 4.8 and section 4.9). Presenting signs and symptoms included reduced level of consciousness and generalised weakness. Ibuprofen induced renal tubular acidosis should be considered in patients with unexplained

hypokalaemia and metabolic acidosis.

- **Opioid use disorder (abuse and dependence):**

  Tolerance, physical and psychological dependence and opioid use disorder (OUD) may develop upon repeated administration of opioids such as codeine. Abuse or intentional misuse of Ibuprofen and Codeine Tablets may result in overdose and/or death.

  Serious clinical outcomes, including fatalities, have been reported in association with abuse and dependence with codeine/ibuprofen combinations, particularly when taken for prolonged periods at higher than recommended doses. These have included reports of gastrointestinal perforations, gastrointestinal haemorrhages, severe anaemia, renal failure, renal tubular acidosis and severe hypokalaemia associated with the ibuprofen component.

  Patients should be informed about the risks and signs of OUD as well as serious clinical outcomes. If these signs occur, patients should be advised to contact their doctor.

  Withdrawal symptoms, such as restlessness and irritability may occur once the drug is stopped.

4.5 Interaction with other medicines and other forms of interaction

- Anti-hypertensives, beta-blockers and diuretics: **BETAPROFEN® 200** may reduce the effect of anti-hypertensives, such as ACE inhibitors, beta-blockers and diuretics.
- 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: **BETAPROFEN® 200** may enhance the effects of anti-coagulants such

as warfarin.

- Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRs): increased risk of gastrointestinal bleeding.
- Diuretics can also increase the risk of nephrotoxicity of **BETAPROFEN® 200.**
- Digoxin: **BETAPROFEN® 200** may exacerbate cardiac failure, reduce GFR and increase plasma digoxin levels.
- Lithium: Decreased elimination of lithium.
- Ciclosporin: Increased risk of nephrotoxicity.
- Mifepristone: A decrease in the efficacy of the medicinal product can theoretically occur due to the antiprostaglandin properties of **BETAPROFEN® 200.** Limited evidence suggests that coadministration of **BETAPROFEN® 200** on the day of prostaglandin administration does not adversely influence the effects of mifepristone or the prostaglandin on cervical ripening or uterine contractility and does not reduce the clinical efficacy of medicinal termination of pregnancy
- Quinolone antibiotics: Patients taking **BETAPROFEN® 200** and quinolones may have an increased risk of developing convulsions.
- Aminoglycosides: **BETAPROFEN® 200** may decrease the excretion of aminoglycosides.
- Herbal extracts: Ginkgo biloba may potentiate the risk of bleeding with **BETAPROFEN® 200.**

4.6 Fertility, pregnancy and lactation

Pregnant women should not use **BETAPROFEN® 200** 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)**.**

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable Effects

SIDE EFFECTS

System Organ Class	Frequent	Less frequent	Frequency Unknown
Blood and lymphatic system disorders		Anaemia, thrombocytopaenia, neutropaenia, eosinophilia, agranulocytosis	

Immune system disorders		aseptic meningitis, angioedema, anaphylaxis, fever, rashes, exacerbation of asthma and bronchospasm	
Psychiatric disorders	Depression		
Nervous system disorders	Dizziness, nervousness, tinnitus, drowsiness, insomnia		
Eye disorders			Visual impairment, changes in visual colour perception, toxic amblyopia.
Cardiac Disorders			Oedema, hypertension and cardiac failure

Gastrointestinal disorders	Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis, Crohn's disease and gastritis.	Abdominal discomfort or pain, gasto-intestinal ulcers, sometimes with bleeding.	
Hepato-biliary disorders		Hepatotoxicity, abnormalities in liver function tests	

Skin and subcutaneous tissue disorders			Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis. Drug reaction with Eosinophillia and Systemic Symptoms (DRESS) [see section 4.4]
Renal and Urinary disorders		Acute renal failure, cystitis, haematuria, intestinal nephritis, nephrotic syndrome.	Renal tubular acidosis*
Metabolism and Nutrition Disorders			Hypokalaemia*

Description of Selected Adverse Reactions:

*Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting typically following prolonged use of ibuprofen at higher than recommended doses when taken together with codeine containing medicines due to dependence on the codeine medicine.

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 Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

The most likely symptoms are epigastric pain and nausea. If recently taken, gastric lavage will remove any unabsorbed ibuprofen. Electrolytes may be corrected by intravenous infusions, if necessary. There is no specific antidote to **BETAPROFEN® 200**.

Treatment is symptomatic and supportive.

Symptoms:

In serious poisoning metabolic acidosis may occur and the prothrombin time/INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute 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).

Exacerbation of asthma is possible in asthmatics.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.3.1 Antirheumatics (anti-inflammatory agents).

ATC Code: M01A E01

Pharmacotherapeutic group: Anti-inflammatory and anti-rheumatic product, non-steroid, propionic acid derivative.

Chemically, Ibuprofen is described as 2-(4-isobutlyphenyl) and is a

propionic acid derivative and has anti-inflammatory, analgesic and antipyretic 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

Tablet Core

Ludipress, magnesium Stearate, microcrystalline cellulose (Avicel),

starch 1500 (pregelatinised Starch)

Tablet Coating

- Dusting powder: acacia, calcium carbonate, purified talc, titanium dioxide
- Gelatin Solution: alcohol 96 % *v/v*, gelatin, nipastat, sucrose
- Opalux Pink Colour: opalux pink A.S 1181, syrup simplex (sucrose and purified water)
- Opaseal P17-0200: alcohol 96 % *v/v*, opadry oy-28-0200
- Polishing wax: carnuba wax, white beeswax
- Purified talc
- Solvent 45

6.2 Incompatibilities

Not applicable

6.3 Shelf life

60 Months – Containers of 20, 30, 100, 500 and 1000 tablets.

24 Months – Blister Pack of 20's.

15 Months – Patient ready packs of different pack sizes.

6.4 Special precautions for storage

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

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

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

Blister Pack of 20's.

Patient ready packs of different pack sizes.

6.6 Special precautions for disposal and other handling

No special requirement for disposal

7. HOLDER OF CERTIFICATE OF REGISTRATION

RANBAXY PHARMACEUTICALS (PTY) LTD

14 Lautre Road,

Stormill, Ext.1,

Roodepoort, 1724

South Africa

8. REGISTRATION NUMBERS

X/3.1/366

Botswana List No.: B9314870

NS2 04/3.1/1627 (Namibia)

9. DATE OF FIRST AUTHORISATION

The date on the registration certificate of the medicine:

22 October 1990

10. DATE OF REVISION OF THE TEXT

20 June 2024