

Professional Information for IBUPROFEN 200 BIOTECH**SCHEDULING STATUS**

S3

1. NAME OF THE MEDICINE

IBUPROFEN 200 BIOTECH tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200 mg ibuprofen.

Excipient with known effect:

Contains sugar (30,0 mg lactose monohydrate per tablet).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

Round biconvex, pink film-coated tablets.

4. CLINICAL PARTICULARS**4.1 Therapeutic indications**

IBUPROFEN 200 BIOTECH is indicated for the treatment of mild to moderate pain of inflammatory origin and fever, including:

- Soft tissue injuries such as sprains and pains
- Headache
- Back pain of musculo-skeletal origin
- Fever
- Muscular aches and pains
- Menstrual pain

- Dental pain
- Pain associated with migraine
- Earache.

4.2 Posology and method of administration

Posology:

Adults and children over 12 years:

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

The recommended dosage of IBUPROFEN 200 BIOTECH is 1 200 mg daily in divided doses (1 to 2 tablets every four hours) for the relief of:

1) Mild to moderate pain of:

- Soft tissue injuries such as sprains and strains
- Dental pain
- Back pain of musculo-skeletal origin
- Earache
- Pain associated with migraine
- Muscular aches and pains.

2) Fever

3) Menstrual pain

Do not exceed 6 tablets (1 200 mg) in any 24 hours.

Once the acute phase has been brought under control, it is normal practice to revert to a maintenance dosage.

If symptoms persist for more than 7 days, consult your doctor.

Children:

Not to be given to children under 12 years.

Method of administration:

For oral use.

Take IBUPROFEN 200 BIOTECH with or immediately after a meal.

4.3 Contraindications

- Hypersensitivity to ibuprofen, aspirin, any other non-steroidal anti-inflammatory medicine (NSAID), or to any of the excipients listed in section 6.1. Because of the possibility of cross-sensitivity due to structural relationships which exist among NSAIDs, allergic reactions may be more likely to occur in patients who have exhibited allergic reactions to these medicines.
- IBUPROFEN 200 BIOTECH is contraindicated during the third trimester of pregnancy and during labour. There is a risk of fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment (refer to section 4.6).
- Peptic ulceration.
- History of gastrointestinal perforation, ulceration or bleeding (PUB) related to previous NSAID use.
- Active or history of recurrent ulcer, haemorrhage, or perforations.
- IBUPROFEN 200 BIOTECH is contraindicated in patients with heart failure, cardiovascular disease or a history of such disorders.
- IBUPROFEN 200 BIOTECH is contraindicated in patients with renal failure.

4.4 Special warnings and precautions for use

Severe hypokalaemia and renal tubular acidosis have been reported due to prolonged use of ibuprofen, as contained in IBUPROFEN 200 BIOTECH, at higher than recommended doses (see sections 4.8 and 4.9). Presenting signs and symptoms included reduced level of consciousness and generalised weakness. NSAID-induced renal tubular acidosis should be considered in patients with unexplained hypokalaemia and metabolic acidosis.

Caution is required with certain conditions:

- Systemic lupus erythematosus as well as those with mixed connective tissue disease due to increased risk of aseptic meningitis (see section 4.8).
- Gastrointestinal (GI) disorders and chronic inflammatory intestinal disease (ulcerative colitis,

Crohn's disease) as these conditions may be exacerbated (see section 4.8).

- Caution is required prior to starting treatment in patients with a history of hypertension.
- Patients undergoing therapy with IBUPROFEN 200 BIOTECH may need to be monitored for the development of blood, kidney, liver or eye disorders.
- Hepatic dysfunction (see section 4.8).

Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration to control symptoms (see GI and cardiovascular risks below).

IBUPROFEN 200 BIOTECH should be used with caution in the elderly. The elderly is at increased risk of the serious consequences of adverse reactions especially GI bleeding and perforation which may be fatal.

Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma or allergic disease.

Cardiovascular and cerebrovascular effects:

Clinical studies suggest that use of ibuprofen, particularly at high doses (2 400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke).

Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g., $\leq 1\ 200$ mg daily) is associated with an increased risk of arterial thrombotic events.

Careful consideration should also be exercised before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g., hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2 400 mg/day) are required.

Gastrointestinal conditions:

Gastrointestinal (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 effects (including ulcerative colitis, Crohn's disease).

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should not use IBUPROFEN 200 BIOTECH.

Caution should be advised in patients receiving concomitant medications which could increase the risk of gastrotoxicity or bleeding, such as corticosteroids, or anticoagulants such as warfarin, selective serotonin uptake inhibitors or antiplatelet medicines such as aspirin (see section 4.5).

Where GI bleeding or ulceration occurs in patients receiving ibuprofen, the treatment should be withdrawn immediately.

Severe skin reactions:

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 for 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. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. IBUPROFEN 200 BIOTECH should be discontinued at the first appearance of signs and symptoms of severe skin reactions, such as 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 taking NSAIDs such as IBUPROFEN 200 BIOTECH. 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 IBUPROFEN 200 BIOTECH and evaluate the patient immediately.

Masking of symptoms of underlying infections:

IBUPROFEN 200 BIOTECH can mask symptoms of infection such as fever and inflammation, which may lead to delayed initiation of appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to varicella. When IBUPROFEN 200 BIOTECH is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

IBUPROFEN 200 BIOTECH contains lactose. Patients with rare hereditary problems of galactose intolerance e.g., galactosemia, the Lapp lactase deficiency or glucose-galactose malabsorption should not take IBUPROFEN 200 BIOTECH.

4.5 Interaction with other medicines and other forms of interaction

- IBUPROFEN 200 BIOTECH may possibly enhance the effects of oral anticoagulants (such as warfarin) and increase the plasma concentrations of lithium, methotrexate and cardiac glycosides. NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside (digoxin) levels.
- There is an increased risk of gastrointestinal bleeding when IBUPROFEN 200 BIOTECH is used with anti-platelet medicines and selective serotonin-reuptake inhibitors (SSRIs) (see section 4.4).
- The risk of nephrotoxicity may be increased if given with angiotensin-converting enzyme inhibitors, ciclosporin, tacrolimus or diuretics.
- There may also be an increased risk of hyperkalaemia with angiotensin-converting enzyme inhibitors and potassium-sparing diuretics.
- The antihypertensive effects of some antihypertensive medicines, including angiotensin converting

enzyme inhibitors, beta-blockers and diuretics may be reduced.

- Convulsions may occur due to interaction with quinolones.
- IBUPROFEN 200 BIOTECH may enhance the effects of phenytoin and sulphonylurea antidiabetics.
- Concomitant administration of IBUPROFEN 200 BIOTECH and aspirin (acetylsalicylic acid) is not generally recommended (unless low-dose aspirin, not above 75 mg daily, has been advised by a doctor) as this combination may increase the risk of adverse reactions (see section 4.4). Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose aspirin (acetylsalicylic acid) on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of IBUPROFEN 200 BIOTECH may reduce the cardioprotective effect of low-dose aspirin (acetylsalicylic acid) cannot be excluded. No clinically relevant effect is likely for occasional IBUPROFEN 200 BIOTECH use (see section 5.1).
- The concomitant use of more than one NSAID, including cyclooxygenase-2 selective inhibitors, should be avoided because of the increased risk of adverse effects (see section 4.4).
- The risk of gastrointestinal perforation, bleeding and ulceration side effects is increased when used with corticosteroids (see section 4.4).
- Alcohol may increase the risk of gastrointestinal side effects, including ulceration or haemorrhage.
- NSAIDs such as IBUPROFEN 200 BIOTECH should not be used for 8 - 12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
- There is an increased risk of haemarthroses and haematoma in HIV positive haemophiliacs receiving concurrent treatment with zidovudine and IBUPROFEN 200 BIOTECH.
- IBUPROFEN 200 BIOTECH may decrease the excretion of aminoglycosides.
- Ginkgo biloba may potentiate the risk of bleeding with IBUPROFEN 200 BIOTECH.

4.6 Fertility, pregnancy and lactation

Pregnancy:

IBUPROFEN 200 BIOTECH is contraindicated during the third trimester of pregnancy and labour. There is a risk of fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment (refer to section 4.4).

Regular use of NSAIDs (as contained in IBUPROFEN 200 BIOTECH) during the third trimester of pregnancy may result in premature closure of the fetal ductus arteriosus in utero and possibly in persistent pulmonary hypertension of the newborn. The onset of labour may be delayed, and its duration increased.

Lactation:

Safety and efficacy have not been established during lactation.

It appears that IBUPROFEN 200 BIOTECH appears in the breast milk.

Fertility:

There is some evidence that medicines, which inhibit cyclooxygenase/ prostaglandin synthesis, may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

4.7 Effects on ability to drive and use machines

IBUPROFEN 200 BIOTECH may cause side effects such as dizziness, drowsiness, fatigue and visual disturbances which can affect the ability to drive a vehicle and use machines (see section 4.8).

Caution is advised before driving a vehicle or operating machinery until the effects of IBUPROFEN 200 BIOTECH are known.

4.8 Undesirable effects

Tabulated list of adverse reactions:

System organ class	Frequency	Adverse reactions
Infections and infestations	Less frequent	Aseptic meningitis.
Blood and the lymphatic system disorders	Less frequent	Thrombocytopenia, anaemia, haemolytic anaemia, aplastic anaemia, leucopenia, pancytopenia, neutropenia, eosinophilia and

			agranulocytosis.
			Inhibition of platelet aggregation is reversible.
Immune system disorders	Less frequent		Anaphylaxis, angioedema, severe shock, aseptic meningitis, hypersensitivity reactions with fever, urticaria and pruritis. Exacerbation of asthma and bronchospasm. 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.
Metabolism and nutrition disorders	Less frequent		Isolated reports in patients with pre-existing renal disease who develop severe hyponatremia and symptoms of severe water intoxication. All symptoms resolve on discontinuation.
Psychiatric disorders	Less frequent		Nervousness and depression.
Nervous system disorders	Frequent		Dizziness, drowsiness and insomnia.
	Less frequent		Headache.
Eye disorders	Less frequent		Decreased visual acuity and visual-field defects, visual impairment, changes in visual colour perception, toxic amblyopia. Prolonged treatment will require regular ophthalmological examinations.
Ear and labyrinth disorders	Less frequent		Tinnitus and vertigo.
Cardiac disorders	Less frequent		Cardiac failure.
Vascular disorders	Less frequent		Hypertension.
Respiratory, thoracic and	Less frequent		Asthma, bronchospasm, dyspnea and wheezing.

mediastinal**disorders****Gastrointestinal disorders:**

Frequent:

Ulcerative stomatitis, dyspepsia, nausea, vomiting, constipation, gastrointestinal haemorrhage/bleeding, haematemesis (sometimes fatal), melaena, diarrhoea, flatulence, abdominal pain, abdominal distension, peptic ulcers and perforation, mouth ulcers, gastritis, exacerbation of colitis and Chron's disease.

Hepato-biliary disorders

Less frequent

Hepatotoxicity, liver disorders (especially in long-term treatment), hepatitis and jaundice.

Abnormalities in hepatic (liver) function tests. Increased values for serum transaminases, serum glutamic pyruvic transaminase, bilirubin and alkaline phosphatase has been reported but have often returned to normal, despite continued treatment.

Skin and subcutaneous tissue disorders

Less frequent

Skin rashes, bullous reactions including erythema multiforme, StevensJohnson syndrome and toxic epidermal necrolysis.

Frequency unknown

Drug reaction with eosinophilia and systemic symptoms (DRESS), AGEP (acute generalised exanthematous pustulosis), photosensitivity reactions.

Renal and urinary disorders

Less frequent

Oedema, acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea, increase in serum creatinine concentrations, and nephrotic syndrome. Cystitis, haematuria, proteinuria and tubulointerstitial nephritis. Acute flank pain and reversible

renal dysfunction have been reported.

General disorders Less frequent Oedema, peripheral oedema.

and administration

site conditions

Investigations: Less frequent Decreased haematocrit and haemoglobin levels.

Post-marketing experience:

System organ class Frequency unknown

Metabolism and nutrition disorders Hypokalaemia*

Renal and urinary disorders Renal tubular acidosis*

*See sections 4.4 and 4.9.

Description of selected adverse reactions:

Drug reaction with eosinophilia and systemic symptoms (DRESS) (see section 4.4).

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of IBUPROFEN 200 BIOTECH is important. It allows continued monitoring of the benefit/ risk balance of IBUPROFEN 200 BIOTECH. Health care providers are asked to report any suspected adverse reactions to the South African Health Products Regulatory Authority (SAHPRA) via the “**Adverse Drug Reactions Reporting Form**”, found online under SAHPRA’s publications: <https://www.sahpra.org.za/Publications/Index/8>.

4.9 Overdose

Symptoms:

The most likely symptoms of overdosage are epigastric pain, nausea, vomiting and rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as vertigo, headache, respiratory depression,

dyspnoea, drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning, hypotension, hyperkalaemia, and 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. Exacerbation of asthma is possible in asthmatics.

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 sections 4.4 and section 4.8).

Management:

Electrolytes may be corrected by intravenous infusions if necessary. Dialysis may be done as IBUPROFEN 200 BIOTECH is not strongly protein bound. There is no specific antidote to IBUPROFEN 200 BIOTECH.

Treatment is symptomatic and supportive and include maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

5. PHARMACOLOGICAL PROPERTIES**5.1 Pharmacodynamic properties**

Category and class: A 2.7 Antipyretic or antipyretic and anti-inflammatory analgesics.

Pharmacotherapeutic group and ATC code: Propionic acid derivatives, M01AE.

Ibuprofen is a non-steroidal compound (phenylpropionic acid derivative NSAID) with analgesic, anti-inflammatory and antipyretic activities. Ibuprofen has demonstrated its efficacy by inhibition of prostaglandin synthesis.

Furthermore, ibuprofen reversibly inhibits platelet aggregation.

5.2 Pharmacokinetic properties

Ibuprofen is rapidly absorbed following administration and is rapidly distributed throughout the whole body.

The excretion is rapid and complete via the kidneys with no evidence of accumulation. Two major metabolites of ibuprofen have been isolated from human urine. They are (+)2-4'hydroxy-2-methylpropyl) phenylpropionic acid (metabolite A) and (+)2,4'(2-carboxylpropyl) phenylpropionic acid (metabolite B).

The levels in human serum of both metabolites have been measured after single and repeated doses. About 60 % of a dose is excreted in the urine, and the excretory products are in the form of either free or conjugated metabolites A and B. No ibuprofen is found.

Maximum plasma concentrations are reached 45 minutes after ingestion if taken on an empty stomach. When taken with food, peak levels are observed after 1 to 2 hours. These times may vary with different dosage forms.

The half-life of ibuprofen is about 2 hours.

Ibuprofen appears in the breast milk in very low concentrations.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Lactose monohydrate

Magnesium stearate (E572)

Maize starch

Polyvinylpyrrolidone (Povidone K30)

Sodium starch glycollate (Explotab).

Tablet coating:

Tabcoat TC-54005 Pink consisting of:

- Hypromellose
- Lactose monohydrate
- Titanium dioxide (E 171)
- Triacetin
- Erythrosine aluminium lake.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store in a well closed container at or below 25 °C.

6.5 Nature and contents of container

Blisters, securitainers, HDPE bottles, sealed aluminum bags (PRP's) and amber glass bottles, which may contain either 10, 15, 20, 28, 30, 56, 84, 90, 100, 500 or 1 000 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Biotech Laboratories (Pty) Ltd

Ground Floor, Block K West, Central Park

400 16th Road, Randjespark, Midrand, 1685

South Africa

8. REGISTRATION NUMBER

V/2.7/224

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18 August 1998

10. DATE OF REVISION OF THE TEXT

24 October 2023