PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1 NAME OF THE MEDICINE

FEVATRIN 100 mg/5 mL oral suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL contains ibuprofen 100 mg.

Preservative: sodium benzoate 10 mg per 5 mL

Contains sugar: sucrose 1 500 mg per 5 mL

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral suspension.

Orange colour suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of symptoms of fever, pain and inflammation, associated with cold and flu, a sore throat, earache, headache, dental pain and minor aches and sprains.

4.2 Posology and method of administration

Posology

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

The dosage of FEVATRIN is 20 mg/kg of body weight per day given in divided doses.

Do not give to children less than 7 kg or under 12 months of age, except on the advice of your doctor.

Children

Pain

Initial dose 5 mg/kg of body weight.

A second dose of 5 mg/kg may be given after 2 hours if pain is not controlled, thereafter 5 mg/kg every 6 hours.

DO NOT EXCEED a total dose of 20 mg/kg of body weight per day.

Fever

5 mg/kg of body weight every 6 hours

DO NOT EXCEED a total dose of 20 mg/kg of body weight per day.

If pain or fever persists for more than 3 days, a doctor should be consulted.

Age	**Body weight**	**Daily dosage**
1 - 2 years	7 – 12 kg	2,5 mL (half medicine measure) up to 3 – 4 times daily
3 – 7 years	14 – 23 kg	2,5 – 5 mL (half to one medicine measure) up to 3 – 4 times daily
8 – 12 years	25 – 40 kg	10 mL (two medicine measures) up to 3 – 4 times daily

Adult:

The initial dose is 400 mg (20 mL), then if necessary 200 mg or 400 mg (10 mL or 20 mL) every four hours. A total dose of 1 200 mg (60 mL) in any 24 hours should not be exceeded.

Method of administration

For oral administration.

A measuring cup is provided in the package. Use this measuring cup to give the amount mentioned in the table above.

4.3 Contraindications

- Hypersensitivity to ibuprofen or to any of the excipients (see section 6.1).
- Patients who have previously shown hypersensitivity reactions (e.g., asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, acetylsalicylic acid (aspirin) or other non-steroidal anti-inflammatory drugs (NSAIDs). 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.
- Active or a history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- History of gastrointestinal perforation, ulceration, or bleeding (PUBs) related to previous NSAIDs, including FEVATRIN.
- Severe hepatic failure, renal failure or heart failure (see section 4.4).
- Pregnancy and lactation (see section 4.6).
- Aspirin-induced nasal polyps associated with bronchospasm
- Uncontrolled asthma
- Children under the age of 1 year
- Porphyria
- Concomitant treatment with lithium
- Concomitant treatment with digoxin.
- Heart failure.

4.4 Special warnings and precautions for use

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

The elderly have an increased frequency of adverse reactions to NSAIDs, including FEVATRIN, especially gastrointestinal bleeding, ulceration and perforation which may be fatal.

Respiratory

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

Other NSAIDs

The use of Ibuprofen with concomitant NSAIDs including cyclo-oxygenase-2 selective inhibitors should be avoided (see section 4.5).

SLE and mixed connective tissue disease

Systemic lupus erythematosus and mixed connective tissue disease, due to increased risk of aseptic meningitis (see section 4.8).

Cardiovascular and cerebrovascular effects

Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure as fluid retention, hypertension and oedema have been reported in association with NSAID therapy.

In view of the FEVATRIN'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

FEVATRIN after careful consideration.

Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at high doses (2 400 mg daily) and in long-term treatment 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., ≤ 1 200 mg daily) is associated with an increased risk of myocardial infarction.

Renal

Renal impairment as renal function may further deteriorate. There is a risk of renal impairment in dehydrated children (see section 4.3 and 4.8). Renal tubular acidosis and hypokalaemia may occur following acute overdose and in patients taking ibuprofen products over long periods at high doses (typically greater than 4 weeks), including doses exceeding the recommended daily dose.

Hepatic

Hepatic dysfunction (see sections 4.3 and 4.8).

Impaired female fertility

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

Gastrointestinal effects

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia) as their conditions may be exacerbated (see section 4.8). Gastrointestinal 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 events.

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 commence treatment on the lowest dose available.

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medicines which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or antiplatelet medicines such as acetylsalicylic acid (aspirin) (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving FEVATRIN, the treatment should be withdrawn.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

DRESS has been reported in patients taking NSAIDs such FEVATRIN. 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 FEVATRIN and evaluate the patient immediately.

Dermatological

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. FEVATRIN should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Masking symptoms of underlying infection

This medicine can mask symptoms of infection, 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 this medicine 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.

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissues infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of FEVATRIN in case of varicella.

Pregnancy:

Regular use of NSAIDs such as FEVATRIN 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.

Excipient warning

FEVATRIN contains sucrose.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take FEVATRIN.

4.5 Interaction with other medicines and other forms of interaction

FEVATRIN should be avoided in combination with

Acetylsalicylic acid (aspirin): Unless low-dose aspirin (not above 75 mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (see sections 4.3 and 4.4). FEVATRIN may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly.

Other NSAIDs including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects (see section 4.4).

FEVATRIN should be used with caution in combination with

Anticoagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (see section 4.4).

Antihypertensives (ACE inhibitors and Angiotensin II Antagonists) and diuretics: NSAIDs may diminish the effect of these medicines.

Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Corticosteroids: Increased risk of gastrointestinal perforation, ulceration or bleeding (PUBs) (see section 4.4).

Antiplatelet medicines and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding (see section 4.4).

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Lithium: There is evidence for potential increases in plasma levels of lithium.

Methotrexate: There is a potential for an increase in plasma levels of methotrexate.

Ciclosporin: Increased risk of nephrotoxicity.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Zidovudine: Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk haemarthroses and haematoma in HIV (positive) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen (as in FEVATRIN).

Quinolone antibiotics: Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs (as in FEVATRIN) and quinolones may have an increased risk of developing convulsions.

4.6 Fertility, pregnancy and lactation

Pregnancy

First trimester:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest 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 %. The risk is believed to increase with dose and duration of therapy. 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, all 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 mother and the neonate, at the end of pregnancy, 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.

Consequently, FEVATRIN is contraindicated during pregnancy.

Breastfeeding

FEVATRIN is not recommended during breastfeeding as ibuprofen is excreted in breastmilk in very low concentrations.

Fertility

FEVATRIN may impair female fertility by an effect on ovulation. This is reversible upon withdrawal of treatment.

4.7 Effects on ability to drive and use machines

FEVATRIN may cause side effects such as dizziness, and drowsiness, 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 FEVATRIN are known.

4.8 Undesirable effects

a. Summary of the safety profile

The most frequently observed adverse events are gastrointestinal in nature.

b. Tabulated summary of adverse reactions

Adverse events which have been associated with ibuprofen are given below, tabulated by system organ class and frequency. Frequencies are defined as: frequent, less frequent and frequency unknown (cannot be estimated from the available data). Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

MedDRA system organ class	**Frequency**	**Adverse reactions**
Infections and infestations	Frequency unknown	Exacerbation of infections related inflammation has been described, in exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection.
Blood and lymphatic system disorders	Less frequent	Haematopoietic disorders, leucopenia, thrombocytopenia, pancytopenia, anaemia, agranulocytosis[1] , neutropenia, eosinophilia
Metabolism and nutrition disorders	Frequency unknown	Decreased appetite, hypokalaemia (typically following prolonged use at higher than recommended doses)
Immune system disorders	Less frequent	Hypersensitivity with urticaria and pruritus[2], severe hypersensitivity reactions, including facial, tongue and throat swelling, dyspnoea, tachycardia, and hypotension (anaphylaxis, angioedema or severe shock)[2]
Nervous system disorders	Less frequent	Headache, dizziness, nervousness, tinnitus, depression, drowsiness, insomnia, aseptic meningitis[3]

Cardiac disorders	Frequency unknown	Cardiac failure and oedema[4]
Vascular disorders	Frequency unknown	Hypertension[4]
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea[2]
Gastrointestinal disorders	Less frequent	Abdominal pain, nausea and dyspepsia[5], diarrhoea, flatulence, constipation, vomiting, peptic ulcer, gastrointestinal perforation or gastrointestinal haemorrhage, melaena, haematemesis[6], mouth ulceration, gastritis, exacerbation of colitis and Crohn's disease[7]
Hepato-biliary disorders	Less frequent	Liver disorder, hepatotoxicity, abnormalities in liver function tests
Skin and subcutaneous tissue disorders	Less frequent	Skin rash[2], bullous reactions, including Stevens-Johnson Syndrome, erythema multiforme and toxic epidermal necrolysis[2]
	Frequency unknown	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), acute generalised exanthematous pustulosis (AGEP), photosensitivity reactions
Renal and urinary disorders	Less frequent	Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema[8], cystitis, haematuria, interstitial nephritis, nephrotic syndrome, ureteric colic, dysuria, renal tubular acidosis

		(typically following prolonged use at higher than recommended doses)
	Frequency unknown	Renal insufficiency
Investigations	Less frequent	Decreased haemoglobin

c. Description of selected adverse reactions

[1] First signs are fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.

[2] Hypersensitivity reactions: These may consist of (a) non-specific allergic reactions and anaphylaxis, (b) respiratory tract reactivity, including asthma, aggravated asthma, bronchospasm, and dyspnoea, or (c) various skin reactions, including pruritus, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses, including toxic epidermal necrolysis, Stevens-Johnson Syndrome and erythema multiforme.

[3] The pathogenic mechanism of medicine-induced aseptic meningitis is not fully understood. However, the available data on NSAID-related aseptic meningitis points to a hypersensitivity reaction (due to a temporal relationship with medicine intake, and disappearance of symptoms after medicine discontinuation). Of note, single cases of symptoms of aseptic meningitis (such as stiff neck, headache, nausea, vomiting, fever or disorientation) have been observed during treatment with ibuprofen in patients with existing auto-immune disorders (such as systemic lupus erythematosus and mixed connective tissue disease).

[4] Clinical trial and epidemiological data suggest that use of ibuprofen (particularly at high doses 2 400 mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (e.g., myocardial infarction or stroke), (see section 4.4).

[5] The adverse events observed most often are gastrointestinal in nature.

[6] Sometimes fatal.

[7] See section 4.4.

[8] Especially in long-term use, associated with increased serum urea and oedema. Also includes papillary necrosis.

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 & Quality Problem Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/.

4.9 Overdose

In children, the ingestion of more than 400 mg/kg of ibuprofen may cause symptoms. In adults, the dose response effect is less clear cut. The half-life in overdose is 1,5 – 3 hours.

The most likely symptoms of overdosage are pain in upper, middle region of the stomach and nausea, vomiting and dizziness, headache, diarrhoea, gastrointestinal bleeding. In more serious poisoning, drowsiness, excitation, coma convulsions, metabolic acidosis prolongation of prothrombin time/INR, renal failure, liver damage, and asthma exacerbation may occur.

Management

Management should be symptomatic and supportive and include the maintenance of clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal of 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 bronchospasm.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 2.7 Antipyretic or antipyretic and anti-inflammatory analgesics.

Pharmacotherapeutic Group: Anti-inflammatory and anti-rheumatic products, non-steroids, propionic acid derivative; ATC Code: M01AE01

Ibuprofen relieves pain and reduces fever and inflammation.

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. 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.

In limited studies, ibuprofen appears in the breast milk in very low concentrations.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acesulfame potassium

Anhydrous citric acid

D & C yellow 10

FD & C red 40

Glycerol/Glycerin

Hypromellose

Mix Berry Flavour B1600948

Polysorbate 80

Purified water

Sodium benzoate

Sucrose

Xanthan gum

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

Transparent HDPE bottle with a white opaque child resistant polypropylene closure and clear polypropylene measuring cup.

Pack size is one 120 mL bottle packed in an outer cardboard carton.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Strides Pharma (SA) Pty Ltd

106 16th Road

Building 2

Midrand

8 REGISTRATION NUMBERS

IBUTRIN Suspension: 55/2.7/0276

FEVATRIN Suspension: 55/2.7/0277.276

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 June 2026

10 DATE OF REVISION OF THE TEXT