

Applicant: Reckitt Benckiser Pharmaceuticals (Pty) Ltd  
Product: Strepsils Intensive  
Dosage Form: Lozenges  
Strength: Flurbiprofen 8,75 mg  
PI/PIL Approval: 27 June 2024

**1.3.1.1. PROFESSIONAL INFORMATION FOR STREPSILS  
INTENSIVE**

**SCHEDULING STATUS**

S1

**1. NAME OF THE MEDICINE**

STREPSILS INTENSIVE 8,75 mg Lozenges

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each lozenge contains 8,75 mg flurbiprofen.

Contains 2,3 g of sugar:

Sucrose 1,407 g per lozenge

Glucose 1,069 g per lozenge

For a full list of excipients, see section 6.1

**3. PHARMACEUTICAL FORM**

Lozenges

A round, pale yellow to brown lozenge with a characteristic honey and lemon taste and the S-brand icon intagliated on both sides.

**4. CLINICAL PARTICULARS**

**4.1 Therapeutic indications**

STREPSILS INTENSIVE is indicated for the relief of pain of sore throats. For bacterial sore throat appropriate antibiotics should be prescribed.

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## **4.2 Posology and method of administration**

### **Posology**

Adults and children over 12 years:

One lozenge sucked/dissolved slowly in the mouth every 3-6 hours as required. Maximum of 5 lozenges in a 24 hour period. It is recommended that this product should not be used for more than 3 days. If symptoms persist, talk to your doctor.

### **Children**

Not indicated for children under 12 years.

### **Elderly**

No dose modification is required.

### **Impaired hepatic function**

STREPSILS INTENSIVE lozenges are contraindicated in patients with severe hepatic impairment (see section 4.3).

### **Impaired renal function**

STREPSILS INTENSIVE lozenges are contraindicated in patients with severe renal impairment (see section 4.3).

### **Method of administration**

For oromucosal administration and short-term use only.

**To avoid local irritation, STREPSILS INTENSIVE lozenges should be moved around the mouth whilst sucking.**

## **4.3 Contra-indications**

- Hypersensitivity to the active substance or to any of the excipients

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- Hypersensitivity to flurbiprofen, aspirin or other NSAIDs.
- Existing or history of peptic ulceration.
- History of bronchospasm, rhinitis or urticaria associated with aspirin or other NSAIDs.
- Pregnancy and lactation (see section 4.6). Avoid use of 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.
- Children under the age of 12 years.
- Severe heart failure, severe renal failure or severe hepatic failure (see section 4.4)
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including STREPSILS INTENSIVE.

#### **4.4 Special warnings and precautions for use**

##### ***Pregnancy***

Use of NSAIDs during the third trimester of pregnancy may result in premature closure of the foetal ductus arteriosus in utero and persistent pulmonary hypertension of the newborn.

Flurbiprofen appears in the breast milk.

Avoid use of 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.

##### ***Respiratory***

Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma. Asthmatics and patients allergic to any other pain relievers should only take STREPSILS INTENSIVE on the advice of a doctor.

##### ***Cardiovascular, Renal and Hepatic Impairment***

NSAIDs have been reported to cause nephrotoxicity in various forms including interstitial nephritis, nephrotic syndrome and renal failure. In patients with renal, cardiac or hepatic impairment, caution

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is required since the use of NSAIDs may result in the deterioration of renal function. Caution is required in patients with hypertension.

### ***Anticoagulant therapy***

Flurbiprofen can prolong bleeding time and caution is required in patients with a potential for abnormal bleeding (such as patients on anticoagulant therapy). Caution is advised in patients with bleeding disorders.

### ***Other NSAIDs***

STREPSILS INTENSIVE should not be taken with other NSAIDs.

### ***Elderly population***

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

### ***Hepatic***

Mild to moderate hepatic dysfunction (see sections 4.3 and 4.8)

### ***Nervous System effects***

Analgesic induced headache - In the event of prolonged use of analgesics or use beyond the regulations headache may occur, which must not be treated with increased doses of the medicinal product.

### ***Gastrointestinal***

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section 4.8)

Gastrointestinal bleeding, ulceration or perforation, which can be fatal has been reported with all NSAIDs at anytime 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, however this effect is not usually seen with short term limited use products such

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as flurbiprofen lozenges.

Patients with a history of GI toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially GI bleeding) to their healthcare professional. Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as acetylsalicylic acid (see section 4.5).

If GI bleeding or ulceration occurs in patients receiving flurbiprofen, the treatment should be withdrawn.

### ***Dermatological***

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported in association with the use of NSAIDs (see section 4.8). Flurbiprofen lozenges should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

### ***Infections***

Since in isolated cases an exacerbation of infective inflammations (e.g. development of necrotising fasciitis) has been described in temporal association with the use of systemic NSAIDs as a class, the patient is advised to consult a physician immediately if signs of a bacterial infection occur or worsen during the flurbiprofen lozenges therapy. It should be considered whether initiation of an anti-infective antibiotic therapy is indicated.

### ***Important Information about some of the ingredients of this medicine***

STREPSILS INTENSIVE contains 1.407 g Sucrose per lozenge and 1.069 g Glucose per lozenge. Patients with rare hereditary problems of fructose intolerance, glucose galactose malabsorption or sucrase isomaltase insufficiency should not take this medicine.

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Contains sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus.

### ***Systemic lupus erythematosus and mixed connective tissue disease***

Patients with systemic lupus erythematosus and mixed connective tissue disease may have an increased risk of aseptic meningitis (see section 4.8), however this effect is not usually seen with short term limited use products such as flurbiprofen lozenges.

### **Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)**

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as STREPSILS INTENSIVE. 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 STREPSILS INTENSIVE and evaluate the patient immediately.

### **4.5 Interaction with other medicines and other forms of interaction**

Studies have shown that the diuretic response to furosemide can occasionally be reduced by flurbiprofen. Similarly, interference with the action of anticoagulants has occasionally been reported. Other studies failed to show any interaction between flurbiprofen and digoxin, tolbutamide or antacids.

**Flurbiprofen should be avoided in combination with:**

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**Other NSAIDs including cyclooxygenase-2 selective inhibitors:** Avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects (esp. gastrointestinal adverse events such as ulcers and bleeding), (see section 4.4).

**Acetylsalicylic acid (low dose):** Unless low-dose aspirin (not above 75mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (see section 4.4).

**Flurbiprofen should be used with caution in combination with:**

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

**Anti-platelet Agents:** Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

**Antihypertensive drugs**

**(Diuretics, ACE inhibitors, angiotensin-II-antagonists):** NSAIDs may reduce the effect of diuretics and other antihypertensive drugs may enhance nephrotoxicity caused by inhibition of cyclooxygenase, especially in patients with compromised renal function (Patients should be adequately hydrated)

**Alcohol:** May increase the risk of adverse reactions, especially of bleeding in the gastrointestinal tract

**Cardiac glycosides:** NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels - adequate control and, if necessary, dose adjustment is recommended

**Ciclosporin:** Increased risk of nephrotoxicity.

**Corticosteroids:** May increase the risk of adverse reactions, especially of the gastrointestinal tract (see section 4.3)

**Lithium:** May increase serum levels of lithium – adequate control and, if necessary, dose adjustment is recommended

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**Methotrexate:** The administration of NSAIDs within 24 hours before or after administration of methotrexate may lead to elevated concentrations of methotrexate and an increase in its toxic effect.

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

**Oral antidiabetics:** Alteration of blood glucose levels reported (increased check rate recommended)

**Phenytoin:** May increase serum levels of phenytoin – adequate control and, if necessary, dose adjustment is recommended

**Potassium sparing diuretics:** Concomitant use may cause hyperkalaemia

**Probenecid Sulfapyrazone:** Medicinal products that contain probenecid or sulfapyrazone may delay the excretion of flurbiprofen.

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

**Selective serotonin reuptake inhibitors (SSRI's):** Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

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

**Zidovudine:** Increased risk of haematological toxicity when NSAIDs are given with zidovudine.

#### **4.6 Fertility, pregnancy, and lactation**

##### **Pregnancy**

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

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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. During the first and second trimester of pregnancy, flurbiprofen should not be given.

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, flurbiprofen is contraindicated during the third trimester of pregnancy.

### **Lactation**

In limited studies, flurbiprofen appears in the breast milk in very low concentration and is unlikely to affect the breast-fed infant adversely. However, because of possible adverse effects of NSAIDs on breast-fed infants, Strepsils Intensive lozenges are not recommended for use in nursing mothers.

### **Fertility**

There is some evidence that drugs which inhibit cyclo-oxygenase/ prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

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#### **4.7 Effects on ability to drive and use machines**

Adverse reactions such as dizziness and somnolence have been reported in patients taking STREPSILS INTENSIVE. If affected, the patient should not drive or operate machinery.

#### **4.8 Undesirable effects**

Hypersensitivity reactions to NSAIDs have been reported and these may consist of:

- (a) non-specific allergic reactions and anaphylaxis
- (b) respiratory tract reactivity e.g. asthma, aggravated asthma, bronchospasm, dyspnoea
- (c) various skin reactions e.g. pruritus, urticaria, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme)

Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment. Clinical trial and epidemiological data suggest that use of some NSAIDs, (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke), (see section 4.4). There is insufficient data to exclude such a risk for flurbiprofen 8.75 mg lozenges

**The following list of adverse effects relates to those experienced with flurbiprofen at OTC doses for short-term use.**

#### **Blood and lymphatic system disorders**

Not known: anaemia, thrombocytopenia.

Less frequent: jaundice, agranulocytosis

#### **Immune System disorders**

Less frequent: anaphylactic reaction

#### **Psychiatric disorders**

Less frequent: insomnia

#### **Cardiovascular and cerebrovascular disorders**

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Not known: Oedema, hypertension and cardiac failure

### **Nervous System disorders**

Frequent: dizziness, headache, parasthesia

Less frequent: somnolence

### **Respiratory, thoracic and mediastinal disorders**

Frequent: throat irritation

Less frequent: exacerbation of asthma and bronchospasm, dyspnoea, wheezing, oropharyngeal blistering, pharyngeal hypoaesthesia.

### **Gastrointestinal disorders**

Frequent: diarrhoea, mouth ulceration, nausea, oral pain, paraesthesia oral, oropharyngeal pain, oral discomfort (warm or burning feeling or tingling of the mouth).

Less frequent: abdominal distension, abdominal pain, constipation, dry mouth, dyspepsia, flatulence, glossodynia, dysgeusia, oral dysaesthesia, vomiting

Not known: gastrointestinal haemorrhage,

### **Hepatobiliary disorders**

Not known: hepatitis

### **Skin and subcutaneous tissue disorders**

Less frequent: various skin rashes, pruritus.

Not known: severe forms of skin reaction such as bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

### **General disorders and administration site conditions**

Less frequent: pyrexia, pain

Not Known: Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) (see section 4.4)

Undesirable effects may be diminished by using the minimum effective dose for the shortest possible duration.

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## **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**

Keep to the stated dose.

### **Symptoms**

Symptoms of overdosage may include nausea, vomiting, headache, drowsiness, blurred vision and dizziness.

### **Management**

Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma. There is no specific antidote to flurbiprofen.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamics properties**

**Pharmacological classification:** A.16. Ear, nose and throat preparations

**Pharmacotherapeutic group:** Throat preparations. ATC Code: R02AX01

Flurbiprofen is non-steroidal anti-inflammatory drug which has analgesic, antipyretic and anti-inflammatory properties. Flurbiprofen is an inhibitor of prostaglandin synthetase enzymes.

### **5.2 Pharmacokinetics properties**

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Flurbiprofen is rapidly absorbed following the use of STREPSILS INTENSIVE with plasma concentrations peaking at 30-40 minutes. Peak concentrations are achieved more rapidly than, but are of similar magnitude to, those achieved after an equivalent swallowed dose.

Flurbiprofen is rapidly distributed throughout the body. It is mainly metabolised by hydroxylation and excreted via the kidneys.

It is extensively bound to plasma proteins and has an elimination half-life of 3 to 6 hours.

Flurbiprofen is excreted in very small amounts in human milk (less than 0,05 microlitres per ml).

### **5.3 Preclinical data**

No preclinical findings of relevance have been reported.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Macrogol 300

Potassium Hydroxide

Lemon flavour 502904 A

Levomenthol

Liquid Glucose

Liquid Sucrose

Honey

### **6.2 Incompatibilities**

Not applicable

### **6.3 Shelf life**

2 years

### **6.4 Special precaution for storage**

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Store at or below 25°C in a dry place, protected from light.

#### **6.5 Nature and contents of container**

Cartons containing 12 blister packed lozenges.

#### **6.6 Special precautions for disposal**

Not applicable

### **7. HOLDER OF CERTIFICATE OF REGISTRATION**

Reckitt Benckiser Pharmaceuticals (Pty) Ltd

8 Jet Park Road

Elandsfontein 1601

### **8 REGISTRATION NUMBER**

35/16/0015

### **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

25 April 2003

### **10. DATE OF REVISION OF THE TEXT**

27 June 2024