

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen 200 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 200 mg of ibuprofen.

Excipient with known effect:

Each film-coated tablet contains lactose monohydrate.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet

Ibuprofen 200 mg:

White coloured round shaped biconvex film-coated tablet debossed '2' on one side and break line on other side. Dimension of the tablet in diameter - 9.60 mm

The score line is to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of migraine-headaches, backache, dental pain, neuralgia and period pains as well as rheumatic and muscular pains.

Ibuprofen tablets relieves pain and reduces inflammation and temperature as well as relieving headaches and other types of pain. It also relieves cold and flu symptoms.

4.2 Posology and method of administration

Method of administration

For oral administration and short-term use only.

During short-term use, if symptoms persist or worsen the patient should be advised to consult a doctor.

Adults and children and adolescents between 12 and 18 years:

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

If in children and adolescents this medicinal product is required for more than 3 days, or if symptoms worsen a doctor should be consulted.

If in adults the product is required for more than 10 days, or if the symptoms worsen the patient should consult a doctor.

Children and Adolescents between 12 and 18 years:

Take 1 or 2 tablets with water, up to three times a day as required.

Adults: Take 1 or 2 tablets with water, up to three times a day as required. Leave at least four hours between doses.

Do not take more than 6 tablets in any 24 hour period.

Not for use by children under 12 years of age.

4.3 Contraindications

Hypersensitivity to ibuprofen or any of the excipients in the product.

Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema, or urticaria) in response to aspirin or other non-steroidal anti-inflammatory drugs.

Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

Severe heart failure (NYHA Class IV), renal failure or hepatic failure (see section 4.4)

Last trimester of pregnancy

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 section 4.2 and GI and cardiovascular risks below).

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

Respiratory

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

Other NSAIDs

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

SLE and mixed connective tissue disease

Systemic lupus erythematosus as well as mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8)

Renal

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

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).

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.

Clinical studies suggest that the use of ibuprofen, particularly at a high dose (2400mg/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. ≤ 1200 mg/day) is associated with an increased risk of arterial thrombotic events.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided. 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 (2400 mg/day) are required.

Cases of Kounis syndrome have been reported in patients treated with ibuprofen. Kounis syndrome has been defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to myocardial infarction.

Impaired female 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.

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).

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 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 the 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 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 aspirin (see section 4.5).

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

Masking of symptoms of underlying infections

Ibuprofen 200 mg film-coated tablets 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 Ibuprofen 200 mg film-coated tablets is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In nonhospital settings, the patient should consult a doctor if symptoms persist or worsen.

Dermatological

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs), including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome), and acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with the use of ibuprofen (see section 4.8). Most of these reactions occurred within the first month.

If signs and symptoms suggestive of these reactions appear ibuprofen should be withdrawn immediately, and an alternative treatment considered (as appropriate).

Information related to excipients

This medicinal product contains lactose monohydrate and should not be given to patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption.

Information on sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

The label will include:

Read the enclosed leaflet before taking this product

Do not take if you:

- have (or have had two or more episodes of) a stomach ulcer, perforation or bleeding
- are allergic to ibuprofen, to any of the ingredients, or to aspirin or other related painkillers
- are taking other NSAID pain killers or aspirin with a daily dose above 75mg

Speak to a pharmacist or your doctor before taking if you:

- have or have had asthma, diabetes, high cholesterol, high blood pressure, a stroke, heart, liver, kidney or bowel problems
- Are a smoker
- Are pregnant

If symptoms persist or worsen, or if new symptoms occur, consult your doctor or pharmacist.

4.5 **Interaction with other medicinal products and other forms of interaction**

The information in this section is based upon previous experience with other NSAIDs. In general, NSAIDs should be used with caution with other drugs that can increase the risk of gastrointestinal ulceration or gastrointestinal bleeding or renal impairment.

Concomitant use not recommended:

Acetylsalicylic acid:

Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects, unless low-dose aspirin (not above 75 mg daily) has been advised by a doctor (see section 4.4).

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose 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 may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

Other NSAIDs including cyclooxygenase-2 selective inhibitors: The concomitant use with other NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided, since simultaneous administration of different NSAIDs can increase the risk of adverse effects (see section 4.4).

Ibuprofen should be used with caution in combination with

Precautions:

Antihypertensives and diuretics

Since NSAIDs may diminish the effects of these drugs. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor or Angiotensin II antagonist and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. These interactions should be considered in patients taking a coxib concomitantly with ACE inhibitors or angiotensin II antagonists. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated, and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Anticoagulants

NSAIDs may enhance the effects of anticoagulants, such as warfarin (see section 4.4).

Cardiac glycosides

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

Ciclosporin

Concomitant administration with NSAIDs may increase the risk of nephrotoxicity.

Tacrolimus

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

Mifepristone

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

Corticosteroids

Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

Lithium

There is evidence for potential increase in plasma levels of lithium.

Methotrexate

There is evidence for the potential increase in plasma levels of methotrexate.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs)

Increased risk of gastrointestinal bleeding (see section 4.4).

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.

Zidovudine (Azidothymidine)

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

There is evidence of an increased risk haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

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, 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 (see section 5.3).

From the 20th week of pregnancy onward, Ibuprofen use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy NSAIDs should not be given unless clearly necessary. If NSAIDs are used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus

constriction should be considered after exposure to Ibuprofen for several days from gestational week 20 onward. Ibuprofen should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension),
- renal dysfunction (see above), which may progress to renal failure with oligohydroamniosis

the mother and the neonate, at the end of pregnancy, to:

- possible prolongation of bleeding time, an antiaggregating effect which may occur even at very low doses,
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, ibuprofen is contraindicated during the third trimester of pregnancy (see section 4.3 and 5.3).

Breast-feeding:

In limited studies, ibuprofen appears in the breast milk in very low concentration and is unlikely to affect the breast-fed infant adversely.

See section 4.4 regarding female fertility.

4.7 Effects on ability to drive and use machines

None expected at recommended dose and duration of therapy.

4.8 Undesirable effects

The list of the following adverse effects relates to those experienced with ibuprofen at OTC doses (maximum 1200mg per day), for short-term use. In the treatment of chronic conditions, under long-term treatment, additional adverse effects may occur.

The adverse events observed most often are gastrointestinal in nature. Adverse events are mostly dose-dependent, in particular the risk of occurrence of gastrointestinal bleeding is dependent on the dosage range and duration of treatment.

Clinical studies suggest that use of ibuprofen, particularly at a high dose 2400mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

Very common	≥1/10
Common	≥1/100 to <1/10
Uncommon	≥1/1000 to <1/100
Rare	≥1/10 000 to <1/1000
Very rare	<1/10 000,
not known	cannot be estimated from the available data

Blood and lymphatic system disorders

Very rare: Haematopoietic disorders (anaemia, leukopenia, thrombocytopenia, pancytopenia, agranulocytosis).

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

Immune system disorders: Hypersensitivity reactions consisting of¹:

Uncommon: Urticaria and pruritus.

Very rare: Severe hypersensitivity reactions. Symptoms could be facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock).

Not known: Respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea.

Psychiatric disorders

Uncommon: Anxiety.

Rare: Psychotic reaction, depression, irritability.

Nervous system disorders

Uncommon: Headache.

Very rare: Aseptic meningitis².

Cardiac disorders

Not known: Cardiac failure and oedema, Kounis syndrome.

Vascular disorders

Not known: Hypertension

Gastrointestinal disorders

Uncommon: Abdominal pain, nausea, dyspepsia.

Rare: Diarrhoea, flatulence, constipation and vomiting.

Very rare: Peptic ulcer, perforation or gastrointestinal haemorrhage, melaena, haematemesis, sometimes fatal, particularly in the elderly. Ulcerative stomatitis, gastritis

Not known: Exacerbation of colitis and Crohn's disease (section 4.4).

Hepatobiliary disorders

Very rare: Liver disorders.

Skin and subcutaneous tissue disorders

Uncommon: Various skin rashes.

Very rare: Severe cutaneous adverse reactions (SCARs) (including Erythema multiforme, exfoliative dermatitis, bullous reactions including Stevens-Johnson Syndrome, and toxic epidermal necrolysis)

Not known: Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), Acute generalised exanthematous pustulosis (AGEP)

Metabolism and Nutrition Disorders

Not known: Decreased Appetite, Hypokalaemia*

Renal and urinary disorders

Very rare: Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema.

Not known: Renal insufficiency, Ureteric colic, dysuria, Renal tubular acidosis*

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

Investigations

Very rare: Decreased haemoglobin levels.

¹Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of (a) non-specific allergic reactions and anaphylaxis, (b) respiratory tract activity comprising asthma, aggravated asthma, bronchospasm, dyspnoea or (c) assorted skin disorders, including rashes of various types pruritus, urticaria, purpura, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

²The pathogenic mechanism of drug-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 drug intake, and disappearance of symptoms after drug 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, mixed connective tissue disease).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

4.9 Overdose

In children ingestion of more than 400 mg/kg may cause symptoms. In adults the dose response effect is less clear cut. The half-life in overdose is 1.5-3 hours.

Symptoms

Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. 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 or overdose may result in and renal tubular acidosis and hypokalaemia. 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.

Management

Management should be symptomatic and supportive and include the 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

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids, propionic acid derivatives.

ATC code: M01AE01

Ibuprofen is a propionic acid derivative NSAID that has demonstrated its efficacy by inhibition of prostaglandin synthesis. In humans, ibuprofen reduces inflammatory pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits platelet aggregation.

Clinical evidence demonstrates that when 400mg of ibuprofen is taken the pain-relieving effects can last for up to 8 hours.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose aspirin (acetylsalicylic acid) on platelet aggregation when they are dosed concomitantly. Some pharmacodynamics studies show that when single doses of ibuprofen 400mg were taken within 8 h before or within 30 min after immediate release aspirin (acetylsalicylic acid) dosing (81mg), a decreased effect of (acetylsalicylic acid) on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of ex vivo data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5).

5.2 Pharmacokinetic properties

Ibuprofen is well absorbed from the gastrointestinal tract. Ibuprofen is extensively bound to plasma proteins.

The median peak plasma concentration for ibuprofen is achieved approximately 1-2 hours after administration. When taken with food, peak plasma levels may be delayed.

Ibuprofen is metabolised in the liver to two major metabolites with primary excretion via the kidneys, either as such or as major conjugates, together with a negligible amount of unchanged ibuprofen. Excretion by the kidney is both rapid and complete.

Elimination half-life is approximately 2 hours.

No significant differences in pharmacokinetic profile are observed in the elderly.

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

5.3 Preclinical safety data

No relevant information, additional to that contained elsewhere in the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Silica, Colloidal anhydrous
Microcrystalline cellulose
Pregelatinized starch (maize)
Sodium starch glycolate
Talc
Magnesium stearate

Film-coating contains:

Hypromellose
Titanium dioxide
Lactose monohydrate
Macrogol 4000
Sodium citrate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

4 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC-Aluminium Blister containing 2, 3, 4, 5, 6, 8, 10, 12, 15, 16 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Strides Pharma UK Ltd.
Unit 4, The Metro Centre,
Dwight Road, Watford,
WD18 9SS
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 13606/0319

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

05/09/2024

10 DATE OF REVISION OF THE TEXT

26/09/2024