

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cuprofen Tablets 400 mg

Ibuprofen Tablets BP 400 mg

Cuprofen Maximum Strength Tablets

Own label: UniChem Extra Strength Ibuprofen 400mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ibuprofen 400 mg

Excipients with known effect:

Lactose: 287mg/tablet

See Section 6.1 for full list of excipients

3 PHARMACEUTICAL FORM

Film-coated tablets (tablets)

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of rheumatic, muscular, dental and period pains and pain in backache, neuralgia, migraine and headache, and for the symptomatic relief of colds, flu and feverishness.

4.2 Posology and method of administration

For oral administration and short-term use only.

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms (see section 4.4).

Adults, the elderly and children and adolescents between 12 and 18 years:

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

Adults should consult a doctor if symptoms persist or worsen, or if the product is required for more than 10 days.

Children and adolescents between 12 and 18 years: One tablet up to three times as day as required.

Adults: One tablet up to three times as day as required.

Leave at least four hours between doses and do not take more than 3 tablets in any 24 hour period.

To be taken preferably after food.

Children under 12 years:

Not to be given to 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, relating to previous NSAIDs therapy.

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

Last trimester of pregnancy (see section 4.6).

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 especially gastrointestinal bleeding 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 Cuprofen Maximum Strength Tablets with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

SLE and mixed connective tissue disease:

Systemic lupus erythematosus and 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:

Cases of Kounis syndrome have been reported in patients treated with Cuprofen Maximum Strength Tablets. 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.

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 use of ibuprofen, particularly at a high dose (2400 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 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.

Impaired female fertility:

There is limited evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible upon 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 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. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose acetylsalicylic acid (aspirin), or other drugs likely to increase gastrointestinal risk (see below and 4.5).

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 medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or antiplatelet agents such as aspirin (see section 4.5).

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

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

Masking of symptoms of underlying infections

This medicinal product 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 pain or fever in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

Excipients

- Lactose - Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this product.
- Sodium – this medicine 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 or any other ingredient of the product, aspirin or other related painkillers
- are taking other NSAID painkillers, or aspirin with a daily dose above 75 mg

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, consult your doctor.

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen should be avoided in combination with:

Aspirin (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 75mg daily) has been advised by a doctor (see section 4.4). Experimental data suggests that ibuprofen may competitively inhibit the effect of low doses 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 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: Avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects (see section 4.4).

Ibuprofen 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 and diuretics: NSAIDs may diminish the effect of these drugs. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

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

Anti-platelet agents 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 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 of haemarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

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.

4.6 Fertility, Pregnancy and lactation

Whilst no teratogenic effects have been demonstrated in animal studies, the use of Cuprofen Maximum Strength Tablets should be avoided during the first 6 months of pregnancy.

During the 3rd trimester, ibuprofen is contraindicated as there is a risk of premature closure of the foetal ductus arteriosus with possible persistent pulmonary hypertension. The onset of labour may be delayed and duration of labour increased with an increased bleeding tendency in both the mother and child. (see section 4.3).

In limited studies, ibuprofen appears in the breast milk in very low concentrations 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 doses and duration of therapy.

4.8 Undesirable effects

Hypersensitivity reactions 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)

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

Hypersensitivity reactions:

Uncommon: Hypersensitivity reactions with urticaria and pruritus.

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

Exacerbation of asthma and bronchospasm.

Gastrointestinal:

The most commonly-observed adverse events are gastrointestinal in nature.

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.

Exacerbation of colitis and Crohn's disease (see section 4.4).

Nervous System:

Uncommon: Headache

Very rare: Aseptic meningitis – single cases have been reported very rarely.

Metabolism and Nutrition Disorders:

Not known: Decreased appetite.

Not known: Hypokalaemia*

Renal:

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

Not known: Ureteric colic, dysuria

Not known: Renal tubular acidosis*

Hepatic:

Very rare: liver disorders.

Haematological:

Very rare: Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.

Skin and subcutaneous tissue disorders:

Uncommon: Various skin rashes

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

Frequency not known:

Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)

Acute generalised exanthematous pustulosis (AGEP)

Photosensitivity reactions

Immune System:

In patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease) during treatment with ibuprofen, single cases of symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been observed (see section 4.4).

Cardiovascular and Cerebrovascular:

Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

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

Not known - Kounis syndrome

Description of Selected Adverse Reactions

*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.

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 via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA yellow card in the Google Play or Apple App store.

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. Exacerbation of asthma is possible in asthmatics.

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).

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

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.

Experimental data suggests 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 hours before or within 30 minutes after immediate release aspirin (acetylsalicylic acid) dosing (81mg), a decreased effect of aspirin (acetylsalicylic acid) on the formation of thromboxane or platelet aggregation occurred. 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 4.5).

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.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Croscarmellose sodium
Methylcellulose
Magnesium stearate
Hypromellose
Talc
Titanium Dioxide
Erythrosine Aluminium Lake
Hydroxypropylmethyl Cellulose

6.2 Incompatibilities

None known.

6.3 Shelf life

Three years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Blister packs comprised of 250.i plain white rigid UPVC and 20p~ hard temper aluminium foil (12, 24, 36, 48.96 tablets)

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Reckitt Benckiser Healthcare (UK) Ltd
Dansom Lane
Hull
HU8 7DS
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 00063/0756

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17/06/2010

10 DATE OF REVISION OF THE TEXT

08/07/2024