SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen 400mg Tablets BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Ibuprofen BP 400mg

Also contains lactose, sucrose and sunset yellow.

For excipients see section 6.1.

3 PHARMACEUTICAL FORM

Tablets

Pink, shiny, biconvex, circular, sugar-coated tablets

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of mild to moderate pain including rheumatic or muscular pain, pain of non-serious arthritic conditions, backache, headache, dental pain, migraine, neuralgia, dysmenorrhoea, feverishness and for the relief of symptoms of colds and influenza.

4.2 Posology and method of administration

For oral administration and short-term use only.

Adults, the elderly and children over 12 years:

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms (see section 4.4). The patient should consult a doctor if symptoms persist or worsen, or if the product is required for more than 10 days.

Not to be used for children under 12 years of age

Ibuprofen 400 mg to be taken up to three times a day as required.

Leave at least four hours between doses and do not take more than 1200 mg in any 24 hour period.

If in children and adolescents between 12 and 18 years this medicinal product is required for more than 3 days, or if symptoms worsen a doctor should be consulted.

Method of administration

For oral administration. To be taken preferably with or after food, with a glass of water. Ibuprofen 400mg tablets should be swallowed whole and not chewed, broken, crushed or sucked on to avoid oral discomfort and throat irritation.

4.3 Contraindications

- Hypersensitivity to Ibuprofen or any of the excipients listed in section 6.1.
- 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 hepatic failure, renal failure or heart 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 Ibuprofen with concomitant NSAIDs including cyclo-oxygenase-2 selective inhibitors should be avoided (see section 4.5).

SLE and mixed connective tissue disease:

Caution is required in certain conditions like systemic lupus erythematosus and mixed connective tissue disease due to increased risk of aseptic meningitis (see section 4.8).

Renal:
Renal impairment as renal function may further deteriorate (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 section 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 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.

Cases of Kounis syndrome have been reported in patients treated with Ibuprofen 400 mg 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.

Impaired female fertility:
There is limited evidence that drugs which inhibit cyclooxygenase/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 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. 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 medications which could increase the risk of gastrotoxicity or bleeding, such as oral corticosteroids, or anticoagulants such as warfarin or selective serotonin reuptake inhibitors or anti-platelet agents such as aspirin (See section 4.5 Interactions).

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

Masking of symptoms of underlying infections:
Ibuprofen 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 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.

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).

Paediatric population:
There is a risk of renal impairment in dehydrated children and adolescents.

Excipients:
Contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactase malabsorption should not take this medicine.

Advice for patients with sugar-related disorders:
Contains Sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

The leaflet will include:

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

If you have been told by your doctor that you have an intolerance to some sugars, talk to your doctor before taking these tablets.

These tablets contain sunset yellow (E110), which can cause allergic-type reactions including asthma. Allergy is more common in those people who are allergic to aspirin.

The label will include:

Please read the enclosed leaflet carefully before taking this medicine.

Do not take if you:
• have ever had a stomach ulcer, perforation or bleeding
• are allergic to ibuprofen (or anything else in this medicine), aspirin or other related painkillers
• are taking other NSAID painkillers, or aspirin with a daily dose above 75mg
• are in the last 3 months of pregnancy

Talk to a pharmacist or your doctor before taking if you:
• have asthma, diabetes, high cholesterol, high blood pressure, had a stroke, liver, heart, kidney or bowel problems
• are a smoker
• are pregnant

If symptoms do not get better, or get worse or if you get new symptoms, talk to your doctor.

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen should not be used in combination with:
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 section 4.4).

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and 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: Increase the 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

Pregnancy
Whilst no teratogenic effects have been demonstrated in animal experiments, the use of Ibuprofen in pregnancy should, if possible, be avoided during the first 6 months of pregnancy.

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, Ibuprofen should not be given unless clearly necessary. If Ibuprofen is 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 3rd trimester, Ibuprofen is contraindicated as there is a risk of premature constriction/closure of the foetal ductus arteriosus with possible persistent pulmonary hypertension and renal dysfunction (see above). The onset of labour may be delayed and the duration increased with an increased bleeding tendency in both the mother and child. (See section 4.3 and 5.3).

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

Fertility
See section 4.4 regarding female fertility.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

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

The list of 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 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) (see section 4.4).

System Organ Class	**Frequency**	**Adverse Event**
Blood and Lymphatic System Disorders	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.
Immune System Disorders		Hypersensitivity reactions consisting of [1]:
	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.
Nervous System Disorders	Uncommon	Headache

	Very rare	Aseptic meningitis[2]
Cardiac Disorders	Not Known	Kounis syndrome, Cardiac failure and oedema,
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 disorder
Skin and Subcutaneous Tissue Disorders	Uncommon	Various skin rashes
	Very rare	Severe cutaneous adverse reactions (SCARs) (including Erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis)
	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)
		Acute generalised exanthematous pustulosis (AGEP)
		photosensitivity reactions
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, Renal tubular acidosis[3]
Investigations	Very rare	Decreased haemoglobin levels
Metabolism and Nutrition Disorders	Not Known	Hypokalaemia[3]

Description of Selected Adverse Reactions

[1] Hypersensitivity 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).

[2]The 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).

[3]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 play store.

4.9 Overdose

Toxicity

Signs and symptoms of toxicity have generally not been observed at doses below 100 mg/kg in children or adults. However, supportive care may be needed in some cases. Children have been observed to manifest signs and symptoms of toxicity after ingestion of 400 mg/kg or greater. 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 significant amounts of ibuprofen will manifest symptoms within 4 to 6 hours.

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, dizziness, occasionally excitation, nystagmus and disorientation or coma. Occasionally patients develop convulsions, fainting,

hypothermia, apnoea and respiratory or CNS depression, cardiovascular toxicity resulting in hypotension, bradycardia or tachycardia. 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.

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.

5.1 Pharmacodynamic properties

ATC Code: M01A E01
Group – Anti-inflammatory and anti-rheumatic products, non-steroids

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

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 hours before or within 30 minutes after immediate release aspirin dosing (81mg), a decreased effect of aspirin on the formation of throm-boxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

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 breast milk in very low concentrations.

5.3 Preclinical safety data

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

6.1 List of excipients

Tablet core:
Lactose, starch, hypromellose, sodium starch glycollate, colloidal anhydrous silica, magnesium stearate.

Tablet coating:
Sucrose, talc, starch, titanium dioxide (E171), Carnauba wax, Mastercote SP0478 (sucrose, titanium dioxide (E171), sunset yellow (E110), erythrosine (E127), sodium benzoate (E211), purified water).

6.2 Incompatibilities

None stated.

6.3 Shelf life

5 years

6.4 Special precautions for storage

Blister pack - This medicinal product does not require any special storage conditions.
Securitainer/Pharmapac bottles – Store below 25°C, Keep the bottle tightly closed.

6.5 Nature and contents of container

Ibuprofen Tablets are available in blister packs of 6, 12, 24, 48, 84 and 96 tablets.

Specification details of blister packs:

PVC (white, rigid, opaque): 250 microns
Aluminium foil (hard tempered): 20 microns
Primer (nitrocellulose): 1.5 -2.5 gsm
Heat seal lacquer: 6.5 - 8.5 gsm

The tablets are also available in a Securitainer pack of 250 and in a Pharmapac bottle of 12.

Specification for Securitainer/Pharmapac: High density polypropylene containers with low density polyethylene caps.

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

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8 MARKETING AUTHORISATION NUMBER(S)

PL 43461/0005

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

22/10/2024