Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:
Hanufen 400mg tablet

2. Qualitative and quantitative composition

Each tablet contains Ibuprofen BP 400mg.

Excipients with known effects

Lactose and sucrose

For excipients see section 6.1

3. Pharmaceutical form
Tablet

4. Clinical particulars

4.1 Therapeutic indications

For the relief of migraine-headaches, backache, dental pain, neuralgia and period pains as well as rheumatic or muscular pains, and pain of non-serious arthritic conditions. Ibuprofen 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

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.

In rheumatic diseases the use of ibuprofen can be required for a longer period. The ibuprofen dose depends on the patient's age and body weight. The maximum single dose for adults should not exceed 800 mg of ibuprofen. The tablet should be swallowed with a glass of water preferably after a meal. It is recommended, that patients with a sensitive stomach take ibuprofen during a meal.

Mild to moderate pain and fever Adults and adolescents ≥40 kg body weight (12 years and above): 200-400 mg given as a single dose or 3-4 times a day with an interval of 6 hours as required. The dosage in migraine headache should be: 400 mg given as a single dose, if necessary 400 mg with intervals up to 6 hours. The maximum daily dose should not exceed 1200 mg.

Children ≥20 kg body weight (6-11 years): Children 20-29 kg (6-9 years): 200 mg 1-3 times a day with intervals of 6 hours as required. The maximum daily dose should not exceed 600 mg. Children 30-90 kg (10-11 years): 200 mg 1-4 times a day with intervals of 6 hours as required. The maximum daily dose should not exceed 800 mg. Ibuprofen is contraindicated in children below 20 kg body weight or younger than 6 years of age. (See section 4.3)

Primary dysmenorrhoea

Adults and adolescents ≥40 kg body weight (12 years of age and above): 200-400 mg 1-3 times a day, with an interval up to 6 hours, as needed. The maximum daily dose should not exceed 1200 mg. Rheumatic diseases Adults: The recommended dose is 1200-1800 mg daily in divided doses.

Maintenance doses of 600 mg1200 mg daily may be effective in some patients. In acute and severe conditions, the dose may be (temporarily) increased to a maximum of 2400 mg in 3 or 4 divided doses.

Adolescents from 15 to 17 years of age: The recommended dose should be adjusted by weight: 20 mg/kg to a maximum of 40 mg/kg body weight daily (max 2400 mg daily) in 3 to 4 divided doses.

Elderly

NSAIDs should be used with particular caution in elderly patients who are more prone to adverse events and are at increased risk of potentially fatal gastrointestinal haemorrhage, ulceration or perforation (see section 4.4). If treatment is considered necessary, the lowest dose for the shortest duration necessary to control symptoms should be used. Treatment should be reviewed at regular intervals and discontinued if no benefit is seen or intolerance occurs.

Impaired renal function

In patients with mild or moderate reduction of renal function, the dose should be kept as low as possible for the shortest duration necessary to control symptoms and renal function monitored. (For patients with severe renal failure see section 4.3).

Impaired liver function

In patients with mild or moderate reduction of liver function the dose should be kept as low as possible for the shortest duration necessary to control symptoms and renal function monitored. (For patients with severe liver failure see section 4.3)

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 required for more than 3 days, or if symptoms worsen a doctor should be consulted.

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)

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. ≤ 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 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 skin reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported rarely in association with the use of NSAIDSs (see section 4.8). Patients appear to be at highest risk of 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. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. Ibuprofen

should be discontinued, at the first appearance of signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.

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 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.

  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 the duration increased with an increased bleeding tendency in both the mother and child. (See section 4.3).

- *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 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).

System Organ Class	**Frequency**	**Adverse Event**
Blood and Lymphatic System Disorders	Very rare	Haematopoietic disorders[1]
Immune System Disorders	Uncommon Very rare	Hypersensitivity with urticaria and pruritus Severe hypersensitivity reactions, including

		facial, tongue and throat swelling, dyspnoea, tachycardia and hypotension (anaphylaxis, angioedema or severe shock)[2]
Nervous System Disorders	Uncommon Very rare	Headache Aseptic meningitis[3]
Cardiac Disorders	Not Known	Cardiac failure and oedema[4]
Vascular Disorders	Not Known	Hypertension
Respiratory, Thoracic and Mediastinal Disorders	Not Known	Respiratory tract reactivity comprising asthma, bronchospasm or dyspnoea[2]
Gastrointestinal Disorders	Uncommon Rare Very rare Not Known	Abdominal pain, nausea and dyspepsia Diarrhoea, flatulence, constipation and vomiting Peptic ulcer, gastrointestinal perforation or gastrointestinal haemorrhage, melaena and haematemesis[6]. Mouth ulceration and gastritis Exacerbation of colitis and Crohn's disease
Hepatobiliary Disorders	Very rare	Liver disorder
Skin and Subcutaneous Tissue Disorders	Uncommon Very rare	Skin rash Bullous reactions, including Stevens-Johnson syndrome,

	Not Known	erythema multiforme and toxic epidermal necrolysis 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[8]
Investigations	Very rare	Haemoglobin decreased

Reporting of suspected adverse reactions
Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

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.

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

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 thromboxane 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 contained elsewhere in the SPC

6. Pharmaceutical Particulars

6.1 List of Excipients

`Maize Starch BP
Dibasic Calcium Phosphate BP
Microcrystalline Cellulose (HiCel 50) BP
Colloidal Anhydrous Silica BP
Povidone USP
Isopropyl Alcohol BP
Purified Water BP
Sodium Starch Glycolate USP
Purified Talc BP
Magnesium Stearate BP
Cross Carmellose Sodium USP
Wincoat F/C In-House
Isopropyl Alcohol BP
Methylene Chloride BP
Lactose
Sucrose

6.2 Incompatibilities

Not applicable

6.3 Shelf-Life

36 months

6.4 Special Precautions for storage

Store below 30°C in a dry place, protect from light.

6.5 Nature and Content of container

Alu- PVC blister of 10 Tablet each, such 10 blisters are packed in a primary carton along with pack insert.

6.6 Special precautions for disposal and other handling

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

7. Marketing Authorization Holder

JOSHPA AFRICA LTD

8. Marketing Authorization Number

CTD9238

9. Date of first authorization/renewal of the authorization

29/06/2023

10. Date of revision of the text

07/05/2025