Summary of Product Characteristics
TRIOFEN-400
(Ibuprofen Tablets BP 400 mg)

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1. Name of the medicinal product

TRIOFEN-400

Ibuprofen Tablets BP 400 mg

2. Qualitative and quantitative composition

Each film-coated tablet contains 400 mg of ibuprofen.

Excipients with known effect
Each film-coated tablet contains methyl parahydroxybenzoate and propyl parahydroxybenzoate, and less than 1 mmol (23 mg) of sodium.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

A pink, circular, biconvex film-coated tablet.

4. Clinical particulars

4.1 Therapeutic indications

TRIOFEN-400 is indicated for the short-term symptomatic treatment of mild to moderate pain, such as headache (including migraine headache), dental pain and primary dysmenorrhoea, and for the reduction of fever.

4.2 Posology and method of administration

Posology
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms. This product is for short-term use only; in adults without medical advice it should not be used for longer than 3 days in migraine headache and fever, or longer than 4 days in pain and dysmenorrhoea. If symptoms persist or worsen, a doctor should be consulted. If an adolescent requires this product for more than 3 days, or if symptoms worsen, a doctor should be consulted.

Mild to moderate pain and fever
Adults and adolescents weighing 40 kg or more (12 years of age and above): 200–400 mg as a single dose or 3 to 4 times daily at intervals of 6 hours as required. For migraine headache: 400 mg as a single dose, followed if necessary by 400 mg at intervals of 6 hours. The maximum daily dose should not exceed 1,200 mg.

Primary dysmenorrhoea

Adults and adolescents weighing 40 kg or more (12 years of age and above): 200–400 mg 1 to 3 times daily at intervals of 6 hours as needed. The maximum daily dose should not exceed 1,200 mg.

Special populations

Paediatric population

Ibuprofen should not be given to children younger than 12 years of age.

Elderly

NSAIDs should be used with particular caution in the elderly, who are more prone to adverse events and at increased risk of potentially fatal gastrointestinal haemorrhage, ulceration or perforation. If treatment is necessary, the lowest dose for the shortest duration should be used, and treatment reviewed at regular intervals.

Renal impairment

In patients with mild or moderate renal impairment, the dose should be kept as low as possible for the shortest duration necessary and renal function monitored.

Hepatic impairment

In patients with mild or moderate hepatic impairment, the dose should be kept as low as possible for the shortest duration necessary and hepatic function monitored.

Method of administration

For oral administration. The tablet should be swallowed with a glass of water during or after a meal; patients with a sensitive stomach are advised to take ibuprofen with food.

4.3 Contraindications

Ibuprofen is contraindicated in patients with:

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1;
- previous hypersensitivity reactions (e.g. asthma, rhinitis, urticaria or angioedema) in response to acetylsalicylic acid or other NSAIDs;
- a history of gastrointestinal bleeding or perforation related to previous NSAID therapy;
- active, or a history of recurrent, peptic ulcer or haemorrhage (two or more distinct episodes of proven ulceration or bleeding);
- severe renal failure or severe hepatic failure;
- severe heart failure (NYHA Class IV);
- significant dehydration (caused by vomiting, diarrhoea or insufficient fluid intake);
- cerebrovascular or other active bleeding;
- unexplained disorders of blood formation;

- the last trimester of pregnancy (see section 4.6);
- children younger than 12 years of age.

4.4 Special warnings and precautions for use

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary. The concomitant use of ibuprofen with other NSAIDs, including cyclo-oxygenase-2 selective inhibitors, should be avoided owing to the increased risk of ulceration or bleeding. Patients on long-term NSAID treatment should undergo regular medical supervision.

Ibuprofen should be administered only after careful consideration of the benefit-risk ratio in patients with systemic lupus erythematosus (SLE) or mixed connective tissue disease, congenital disorders of porphyrin metabolism (e.g. acute intermittent porphyria), the first and second trimester of pregnancy, and during lactation. Special care is required in patients with gastrointestinal disease (including ulcerative colitis and Crohn's disease), cardiac insufficiency and hypertension, reduced renal or hepatic function, disturbed haematopoiesis, blood coagulation defects, allergic conditions or asthma, and immediately after major surgery.

Gastrointestinal bleeding, ulceration and perforation

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 is higher with increasing dose, in patients with a history of ulcer (particularly if complicated by haemorrhage or perforation) and in the elderly, who should commence treatment on the lowest available dose. For these patients, and those requiring concomitant low-dose acetylsalicylic acid or other agents likely to increase GI risk, combination therapy with protective agents (e.g. misoprostol or proton-pump inhibitors) should be considered. Treatment should be withdrawn if GI bleeding or ulceration occurs. Caution is advised in patients receiving concomitant medicinal products that may increase the risk of ulceration or bleeding (e.g. oral corticosteroids, anticoagulants such as warfarin or heparin, selective serotonin reuptake inhibitors, or antiplatelet agents).

Cardiovascular and cerebrovascular effects

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate heart failure, as fluid retention, hypertension and oedema have been reported with NSAID therapy. Clinical studies suggest that high-dose ibuprofen (2,400 mg/day) may be associated with a small increased risk of arterial thrombotic events (e.g. myocardial infarction or stroke); overall, epidemiological data do not suggest such a risk with low-dose ibuprofen (≤ 1,200 mg/day). Patients with uncontrolled hypertension, congestive heart failure (NYHA II–III), established ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease should be treated only after careful consideration, and high doses (2,400 mg/day) avoided. Careful consideration is

also required before initiating long-term treatment in patients with cardiovascular risk factors (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

Kounis syndrome

Cases of Kounis syndrome (acute coronary syndrome secondary to an allergic or hypersensitivity reaction, with coronary artery constriction potentially leading to myocardial infarction) have been reported with ibuprofen.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions, including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalised exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported. Most occur within the first month of treatment. Ibuprofen should be withdrawn immediately at the first appearance of signs or symptoms suggestive of these reactions.

Infections

Use of ibuprofen in patients with varicella is advisable to avoid, as NSAIDs have been associated with serious cutaneous and soft-tissue infectious complications. Ibuprofen may also mask the symptoms of infection (fever, pain, swelling), which may delay appropriate treatment; monitoring of infection is advised when ibuprofen is used for fever or pain related to infection.

Renal effects

Ibuprofen may cause retention of sodium, potassium and fluid, potentially leading to oedema, cardiac insufficiency or hypertension in predisposed patients. Renal tubular acidosis and hypokalaemia may occur after acute overdose or prolonged high-dose use. Cases of acute interstitial nephritis with haematuria and proteinuria, and occasionally nephrotic syndrome, have been reported; patients at greatest risk include those with renal dysfunction, heart failure or hepatic dysfunction, those taking diuretics or ACE inhibitors, and the elderly. Discontinuation is generally followed by recovery.

Other precautions

Severe acute hypersensitivity reactions (e.g. anaphylactic shock) are observed very rarely; treatment must be stopped at the first signs of a hypersensitivity reaction. Bronchospasm, urticaria or angioedema may be precipitated in patients with, or with a history of, bronchial asthma, chronic rhinitis, sinusitis, nasal polyps or allergic disease. Aseptic meningitis has been observed rarely, particularly in patients with SLE or mixed connective tissue disease. Prolonged use of analgesics for headache may worsen it (medication overuse headache), and habitual use of analgesics may cause permanent renal damage. Ibuprofen may temporarily inhibit platelet aggregation and prolong bleeding time; patients with coagulation defects or on anticoagulants should be observed carefully. During long-term treatment, periodic monitoring of hepatic and renal function and blood

counts is advised. Alcohol should be avoided as it may intensify NSAID side effects.

Excipients

This medicinal product contains methyl parahydroxybenzoate and propyl parahydroxybenzoate, which may cause allergic reactions (possibly delayed). It also contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Combinations to avoid or use with caution

- Acetylsalicylic acid: concomitant use is generally not recommended owing to increased adverse effects; ibuprofen may competitively inhibit the effect of low-dose acetylsalicylic acid on platelet aggregation, and regular long-term use may reduce its cardioprotective effect (no clinically relevant effect is likely with occasional use).
- Other NSAIDs, including COX-2 selective inhibitors: concurrent use increases the risk of gastrointestinal ulceration and bleeding and should be avoided.
- Anticoagulants (warfarin, heparin): NSAIDs may enhance their effect; monitor coagulation.
- Antiplatelet agents (e.g. clopidogrel, ticlopidine), corticosteroids and SSRIs: increased risk of gastrointestinal bleeding.
- Methotrexate: NSAIDs may reduce its clearance and increase toxicity; avoid concomitant use with high-dose methotrexate and monitor with low-dose regimens.
- Digoxin, phenytoin and lithium: serum concentrations may be increased with concomitant ibuprofen.
- Diuretics and antihypertensives (including ACE inhibitors, beta-blockers and angiotensin-II antagonists): NSAIDs may reduce their effect and, particularly in patients with reduced renal function, may impair renal function (potentially reversible acute renal failure). Concurrent ACE inhibitors or potassium-sparing diuretics may cause hyperkalaemia; monitor potassium.
- Ciclosporin and tacrolimus: increased risk of nephrotoxicity.
- Aminoglycosides: reduced elimination and increased toxicity.
- Cholestyramine: reduced (by about 25%) and delayed absorption of ibuprofen; administer at least one hour apart.
- CYP2C9 inhibitors (e.g. voriconazole, fluconazole): may increase ibuprofen exposure (by approximately 80–100%); a dose reduction should be considered, particularly with high-dose ibuprofen.
- Zidovudine (increased risk of haematological toxicity/haemarthrosis in haemophiliac patients), ritonavir (may increase NSAID concentrations),

mifepristone (NSAIDs used within 8–12 days may reduce its effect), probenecid or sulfinpyrazone (delayed ibuprofen elimination), quinolone antibiotics (increased risk of convulsions), sulphonylureas (enhanced hypoglycaemic effect), captopril (reduced natriuretic effect), baclofen (increased toxicity), bisphosphonates and pentoxifylline (increased GI risk), and Ginkgo biloba (increased bleeding risk).

4.6 Fertility, pregnancy and lactation

Pregnancy

Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or embryo-foetal development. Epidemiological data suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy (absolute risk of cardiovascular malformation increasing from below 1% to approximately 1.5%), with the risk believed to increase with dose and duration. From the 20th week of pregnancy onward, ibuprofen use may cause foetal oligohydramnios (from foetal renal dysfunction) and ductus arteriosus constriction; antenatal monitoring for these should be considered after use for several days from week 20, and ibuprofen discontinued if they occur. During the first and second trimester, ibuprofen should not be given unless clearly necessary, at the lowest dose and shortest duration. During the third trimester, all prostaglandin synthesis inhibitors may cause foetal cardiopulmonary toxicity (premature closure of the ductus arteriosus and pulmonary hypertension) and renal dysfunction, and may prolong bleeding time and inhibit uterine contractions in mother and neonate; ibuprofen is therefore contraindicated during the last trimester of pregnancy.

Breast-feeding

Ibuprofen is excreted in breast milk, but at therapeutic doses in short-term treatment an effect on the breast-fed infant is unlikely. If longer treatment is prescribed, early weaning should be considered.

Fertility

There is some evidence that medicinal products inhibiting cyclo-oxygenase/prostaglandin synthesis may impair female fertility by an effect on ovulation; this is reversible on withdrawal of treatment.

4.7 Effects on ability to drive and use machines

Ibuprofen generally has no adverse effect on the ability to drive or use machines. However, at high doses, adverse effects such as fatigue, somnolence and vertigo (common) and visual disturbances (uncommon) may occur and may impair the ability to drive or operate machinery in individual cases; this effect is potentiated by concomitant alcohol.

4.8 Undesirable effects

Summary of the safety profile

The most commonly observed adverse reactions are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal

(particularly in the elderly), may occur. Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment, and high-dose ibuprofen (2,400 mg/day) may be associated with a small increased risk of arterial thrombotic events. The stated frequencies refer to short-term use at daily doses up to a maximum of 1,200 mg for oral dosage forms.

Tabulated list of adverse reactions

Frequency categories are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); and not known (cannot be estimated from the available data).

System Organ Class	**Frequency**	**Adverse reactions**
Blood and lymphatic system disorders	Very rare	Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis, neutropenia); first signs may include fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe fatigue, and nasal or skin bleeding
Immune system disorders	Uncommon	Hypersensitivity reactions such as urticaria, pruritus, purpura and exanthema, as well as asthma attacks (sometimes with hypotension)
	Rare	Lupus erythematosus syndrome
	Very rare	Severe hypersensitivity reactions (facial oedema, swelling of the tongue, laryngeal swelling with airway constriction, dyspnoea, tachycardia and hypotension to the point of life-threatening shock)
Psychiatric disorders	Rare	Depression, confusion, hallucinations
	Not known	Anxiety
Nervous system disorders	Uncommon	Headache, somnolence, vertigo, fatigue, agitation, dizziness, insomnia, irritability
	Very rare	Aseptic meningitis
	Not known	Optic neuritis, paraesthesia
Eye disorders	Uncommon	Visual disturbances
	Rare	Toxic amblyopia
Ear and labyrinth disorders	Very rare	Tinnitus
	Not known	Hearing impairment
Cardiac disorders	Very rare	Palpitations, heart failure, myocardial infarction, acute pulmonary oedema, oedema
	Not known	Kounis syndrome
Vascular disorders	Very rare	Hypertension
Respiratory, thoracic and mediastinal disorders	Uncommon	Rhinitis, bronchospasm

System Organ Class	Frequency	Adverse reactions
Gastrointestinal disorders	Common	Gastrointestinal disturbances such as heartburn, dyspepsia, abdominal pain, nausea, vomiting, flatulence, diarrhoea and constipation
	Uncommon	Gastrointestinal ulcers (sometimes with bleeding and perforation), occult blood loss which may lead to anaemia, melaena, haematemesis, ulcerative stomatitis, colitis, exacerbation of inflammatory bowel disease, complications of colonic diverticula (perforation, fistula), gastritis
	Very rare	Oesophagitis, pancreatitis, intestinal strictures
Hepatobiliary disorders	Very rare	Liver dysfunction, liver damage (especially in long-term use), liver failure, acute hepatitis, jaundice
Skin and subcutaneous tissue disorders	Very rare	Severe cutaneous adverse reactions (SCARs), including erythema multiforme, exfoliative dermatitis, bullous reactions (Stevens-Johnson syndrome and toxic epidermal necrolysis), alopecia and necrotising fasciitis
	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP), photosensitivity reactions
Renal and urinary disorders	Rare	Renal papillary necrosis (in long-term use)
	Very rare	Oedema (especially in patients with arterial hypertension or renal insufficiency), nephrotic syndrome, interstitial nephritis which may be associated with renal failure
	Not known	Renal tubular acidosis*
Metabolism and nutrition disorders	Not known	Hypokalaemia*
General disorders and administration site conditions	Not known	Malaise
Investigations	Rare	Increased blood urea nitrogen, serum transaminases and alkaline phosphatase; decreased haemoglobin and haematocrit; inhibition of platelet aggregation; prolonged bleeding time; decreased serum calcium; increased serum uric acid

* Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting, typically following prolonged use 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 to the National Regulatory Authority.

4.9 Overdose

Symptoms

Most patients who ingest clinically important amounts of NSAIDs develop no more than nausea, vomiting, epigastric pain or, more rarely, diarrhoea; nystagmus, blurred vision, tinnitus, headache and gastrointestinal bleeding may also occur. In more serious poisoning, central nervous system toxicity may manifest as vertigo, dizziness, drowsiness, occasionally excitation and disorientation, or loss of consciousness and coma; convulsions may occur, and children may develop myoclonic cramps. Metabolic acidosis, hypothermia, hyperkalaemia and prolongation of the prothrombin time/INR may occur, together with acute renal failure, liver damage, hypotension, respiratory depression and cyanosis; asthma may be exacerbated in asthmatics. Prolonged use at higher than recommended doses, or overdose, may cause renal tubular acidosis and hypokalaemia.

Management

Treatment should be symptomatic and supportive, including maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Activated charcoal (or gastric emptying) is indicated if the patient presents within one hour of ingestion of more than 400 mg/kg body weight. Convulsions, if frequent or prolonged, should be treated with intravenous diazepam or lorazepam, and bronchodilators given for asthma. There is no specific antidote.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-inflammatory and antirheumatic products, non-steroids; propionic acid derivatives. ATC code: M01AE01.

Mechanism of action

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic and antipyretic activity. It inhibits prostaglandin synthesis by inhibiting the activity of cyclo-oxygenase, thereby reducing pain, swelling and fever, and also inhibits ADP- and collagen-stimulated platelet aggregation. Ibuprofen may competitively inhibit the effect of low-dose acetylsalicylic acid on platelet aggregation when dosed concomitantly, and regular long-term use may reduce its cardioprotective effect. By inhibiting prostaglandin synthesis in the uterus, ibuprofen reduces uterine pressure and contractions, which is thought to explain its effect in dysmenorrhoea. Inhibition of renal prostaglandin synthesis may lead to renal insufficiency, fluid retention and heart failure in at-risk patients, and inhibition of prostaglandins involved in ovulation may affect female fertility.

5.2 Pharmacokinetic properties

Absorption
Ibuprofen is rapidly absorbed from the gastrointestinal tract, with peak serum concentrations occurring 1 to 2 hours after administration.

Distribution
Ibuprofen is rapidly distributed throughout the body and is approximately 99% bound to plasma proteins.

Biotransformation
Ibuprofen is metabolised in the liver by hydroxylation and carboxylation to pharmacologically inactive metabolites.

Elimination
The elimination half-life is approximately 2.5 hours in healthy individuals. The (inactive) metabolites are excreted mainly (about 90%) by the kidneys, and also in the bile.

5.3 Preclinical safety data

As a well-established and widely used medicinal product, the preclinical safety of ibuprofen is well documented. Subchronic and chronic toxicity in animals was manifested mainly as gastrointestinal tract damage and ulceration. In vitro and in vivo tests have not shown clinically significant mutagenicity, and no carcinogenic effects were observed in mice or rats. Ibuprofen inhibited ovulation in rabbits and impaired implantation in several animal species; it crossed the placenta in reproduction studies in rats and rabbits, and at maternally toxic doses an increased incidence of malformations (e.g. ventricular septal defects) was observed.

6. Pharmaceutical particulars

6.1 List of excipients

- Dibasic calcium phosphate
- Maize starch
- Microcrystalline cellulose
- Povidone (K30)
- Methyl parahydroxybenzoate
- Propyl parahydroxybenzoate
- Croscarmellose sodium
- Colloidal silicon dioxide
- Purified talc
- Magnesium stearate
- Hypromellose (HPMC)
- Titanium dioxide
- Erythrosine (E127)

- Propylene glycol
- Isopropyl alcohol
- Methylene chloride (dichloromethane)
- Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C. Protect from light. Keep out of the reach of children.

6.5 Nature and contents of container

10 Alu-PVC blisters of 10 tablets each, packed in a printed carton together with a package 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 Authorisation Holder

ZAIN PHARMA LTD

Plot No. 209/13741, Colchester Park, Go-Down No. 1, 2, 3, Off Mombasa Road, P.O. Box 100167-00101, Nairobi, Kenya.

8. Marketing Authorisation Number

CTD12788

9. Date of first authorisation / renewal of the authorisation

03.07.2026

10. Date of revision of the text

02.07.2026