SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ibuject – Ibuprofen 4mg in 1ml Solution for Infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml solution for infusion contains 4mg Ibuprofen

Each 50ml bag contains 200mg Ibuprofen Each 100ml bag contains 400mg Ibuprofen Each 150ml bag contains 600mg Ibuprofen

Excipient(s) with known effect: each 1ml contains approximately 0.17mmol (4mg) sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion Clear and colourless to pale yellow solution. pH: 7.5-8.5 Osmolality: 270-360 mOsm/l.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ibuprofen 200mg Infusion (50ml) is indicated in adolescents and children from 20 kg body weight and 6 years of age and above for the short-term symptomatic treatment of acute moderate pain and for the short-term symptomatic treatment of fever.

Ibuprofen 400mg Infusion (100ml) is indicated in adults for the short-term symptomatic treatment of acute moderate pain, and for the short-term symptomatic treatment of fever

Ibuprofen 600 mg Infusion (150ml) is indicated in adults for the short-term symptomatic treatment of acute moderate pain

Intravenous route od administration must only be used when it is clinically justified and when other routes of administration are not possible.

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 (see section 4.4).

Use should be limited to situations where oral administration is inappropriate. Patients must switch to oral treatment as soon as this is possible.

This medicinal product is indicated for short-term acute treatment only and should not be used for more than 3 days.

Adequate hydration of the patient should be maintained to minimize the risk of possible adverse reactions at renal level.

The dose will be individually adjusted by your doctor, based on your weight and general condition.

For children and adolescents, ibuprofen is dosed depending on body weight or age, 5 to 10 mg/kg body weight as a single dose up to a maximum total daily dose of 30 mg/kg body weight:

The recommended maximum daily dose should not be exceeded.

Recommended Dosage Information

Patient	**Body weight (Kg)**	**Age (Years)**	**Dose (mg)**	**Infusion volume (ml)**	**Frequency**	**Maximum Daily Dose (mg)**
Children	Less than 20	Under 6	**Not Recommended**			
	20 - 29	6 - 9	200	50	Up to 3 times daily	600
	30 - 39	10 - 11	200	50	Up to 4 times daily	800
Adolescents	40 or more	12 - 17	200 – 400	50 - 100	Up to 3 times daily	1200
Adults			400	100	Every 6 – 8 hours as necessary	1200
			600	150		

Elderly Patients

Like with all non-steroidal anti-inflammatory drugs (NSAIDs), precautions should be taken when treating elderly patients, as they are generally more prone to adverse effects (see section 4.4 and 4.8), and are more likely to have renal, hepatic, and cardiovascular dysfunction, and to be using concomitant medications. Specifically, it is recommended to administer the lowest effective dose for the shortest duration necessary to control symptoms for this population. Treatment should be reviewed at regular intervals and discontinued if no benefit is seen, or intolerance occurs.

Renal insufficiency

Precautions should be taken when NSAIDs are used in patients with renal insufficiency. In patients with mild or moderate renal impairment the initial dose should be reduced and be kept as low as possible for the shortest duration necessary to control symptoms and renal function monitored. This medicinal product is contraindicated in patients with severe renal insufficiency (see section 4.3).

Hepatic insufficiency

Precautions should be taken when NSAIDs are used in this population although differences in the pharmacokinetic profile have not been observed. Patients with mild or moderate hepatic insufficiency should start the treatment

with reduced doses, the dose should be kept as low as possible for the shortest duration necessary and they should be carefully monitored. This medicinal product is contraindicated in patients with severe hepatic insufficiency (see section 4.3).

Method of administration

For Intravenous use. This product should only be administered by qualified healthcare professionals in an environment where appropriate equipment is available (during treatment).

The solution should be administered as an intravenous infusion over 30minutes.

4.3 Contraindications

- Hypersensitivity to the active substance, to other NSAIDs or to any of the excipients listed in section 6.1.
- A history of bronchospasm, asthma, rhinitis, angioedema or urticaria associated with taking acetylsalicylic acid (ASA)or other non-steroidal anti-inflammatory drugs (NSAIDs)
- Conditions involving an increased tendency or active bleeding such as thrombocytopenia
- 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
- Cerebrovascular or other active bleeding
- Severe hepatic or renal insufficiency
- Severe heart failure (NYHA Class IV)
- Severe dehydration (caused by vomiting, diarrhoea, or insufficient fluid intake)
- Pregnancy, in the last trimester (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 possible time necessary to control symptoms (see section 4.8). Concomitant use of Ibuprofen Infusion with NSAIDs, including cyclooxygenase-2 selective inhibitors (Coxib), should be avoided. The frequency of the adverse reactions to NSAIDs is increased in elderly patients, especially gastrointestinal bleeding, and perforation, which may be fatal (see section 4.8).

Gastrointestinal risks

GI bleeding, ulceration, or perforation, which can be fatal, have been reported during treatment with all NSAIDs 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 (ASA), or other drugs likely to increase the gastrointestinal risk (see below and section 4.5).

Patients with a history of GI toxicity, particularly in 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 acetylsalicylic acid (ASA) (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving Ibuprofen Infusion, treatment should be withdrawn (see section 4.3).

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).

Cardiovascular and cerebrovascular effects

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). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g., ≤ 1200mg/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.

Severe skin reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported

very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk for 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 medicinal 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.

Hepatic or renal insufficiency

Ibuprofen should be used with caution in patients with a history of liver or kidney disease and especially during simultaneous treatment with diuretics, as the inhibition of prostaglandins can cause fluid retention and renal function impairment. Ibuprofen should be administered in these patients at the lowest dose possible, and patient´s renal function should be regularly monitored.

In case of dehydration, ensure sufficient fluid intake. Use special caution in dehydrated patients, for example due to diarrhoea, such as dehydration could be a trigger factor for the development of kidney failure.

Regular use of analgesics, especially when combining of different analgesic substances, can lead to kidney damage with the risk of renal insufficiency (analgesic nephropathy). This risk is higher in the elderly and patients with renal insufficiency, heart failure, liver dysfunction and those taking diuretics or ACE inhibitors. After discontinuing NSAID therapy, patient´s pre-treatment condition is usually restored.

As with other NSAIDs, ibuprofen can cause mild transient increases in some liver function parameters as well as significant increases in transaminases. If there is a significant increase in these parameters, treatment should be discontinued (see section 4.3).

Anaphylactoid Reactions

As standard practice during intravenous infusion, close patient monitoring is recommended, especially at the beginning of the infusion to detect any anaphylactic reaction caused by the active substance or the excipients. Severe acute hypersensitivity reactions (e.g., anaphylactic shock) are very rarely observed. At the first signs of a hypersensitivity reaction following the administration of Ibuprofen Infusion, therapy must be stopped and symptomatic treatment must be established. Medically required measures, in line with the symptoms, must be initiated by specialist personnel.

Respiratory disorders

Caution is required if this medicinal product is administered to patients suffering from, or with a previous history of, bronchial asthma, chronic rhinitis or allergic diseases since NSAIDs have been reported to cause bronchospasm, urticaria or angioedema in such patients.

Haematological Effects

Ibuprofen may temporarily inhibit the blood-platelet function (thrombocyte aggregation), increasing the bleeding time and the risk of haemorrhage.

Ibuprofen should only be used with particular caution in patients receiving ASA to inhibit platelet aggregation (see sections 4.5 and 5.1).

Patients with coagulation disorders or those undergoing surgery should therefore be monitored. Special medical vigilance is required for use in patients immediately after undergoing major surgery.

During prolonged ibuprofen administration, regular checking of liver values, kidney function, and blood counts is required. Ibuprofen should be used only after strict assessment of the benefit / risk in patients with congenital disorder of porphyrin metabolism (e.g., acute intermittent porphyria). Through concomitant consumption of alcohol, active substance-related undesirable effects, particularly those that concern the gastrointestinal tract or the central nervous system, may be increased on use of NSAIDs.

Caution is required in patients with certain conditions, which may be made worse:

- In patients who react allergically to other substances, as an increased risk of hypersensitivity reactions occurring also exists for them on use of this medicinal product.
- In patients who suffer from hay fever, nasal polyps or chronic obstructive respiratory disorders as an increased risk exists for them of allergic reaction occurring. These may present as asthma attacks (so-called analgesic asthma), Quincke´s oedema or urticaria.

Aseptic Meningitis:

Some cases of aseptic meningitis have been reported with the use of ibuprofen in patients with systemic lupus erythematosus (SLE). Although it is more likely to occur in patients with SLE and related connective tissue diseases, it has also been reported in some patients who do not have any underlying chronic disease. This, therefore, should be considered when administering this treatment (see section 4.8).

Ophthalmological Effects

Blurred or diminished vision, scotomata, and changes in colour vision have been reported with oral ibuprofen. Discontinue ibuprofen if the patient develops such complaints and refer the patient for an ophthalmologic examination that includes central visual fields and colour vision testing.

Others

Prolonged use of painkillers may cause headache that must not be treated with increased doses of the medicinal product.

Exceptionally, varicella can cause serious cutaneous and soft tissues infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of ibuprofen in case of varicella.

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.

Interference with laboratory tests:

- bleeding time (may be extended for a day after discontinuation of therapy)
- blood glucose concentration (may decrease)
- creatinine clearance (may decrease)
- haematocrit or haemoglobin (may decrease)
- blood levels of urea nitrogen and serum creatinine and potassium (may increase)
- with liver function tests: increased transaminase values

Precautions regarding excipients

This medicinal product contains 4mg sodium per 1ml, equivalent to 15% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Other NSAIDs, including COX-2 inhibitors and salicylates:

As a result of synergist effects, the concurrent administration use of two or more NSAIDs may increase the risk of gastrointestinal ulcers and bleeding. Co-administration of ibuprofen with other NSAIDs should therefore be avoided (see section 4.4).

Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects. 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).

Lithium

Co-administration of ibuprofen with lithium preparations can increase the serum level of these medicinal products. Monitoring the serum lithium level is necessary.

Cardiac glycosides (Digoxin)

NSAIDs may exacerbate cardiac failure, reduce glomerular filtration rate, and increase plasma levels of cardiac glycosides. Monitoring of serum digoxin is recommended.

Phenytoin

Plasmatic levels of phenytoin may be increased in the concomitant treatment with ibuprofen and therefore the risk of toxicity may increase.

Antihypertensive (Diuretics, ACE inhibitors, beta-receptor blocking medicines and angiotensin-II antagonists)

Diuretics and ACE-inhibitors may increase the nephrotoxicity of NSAIDs. NSAIDs can reduce the effect of diuretics and other antihypertensive drugs, including ACE-inhibitors and beta-blockers. In patients with reduced kidney function (e.g., dehydrated patients or elderly patients with reduced kidney function) the concomitant use of an ACE inhibitor and angiotensin-II antagonists with a cyclo-oxygenase-inhibiting medicinal product can lead to further impairment of kidney function, and up to acute renal failure. This is usually reversible. Such combinations should, therefore, only be used with caution, especially in elderly patients. Patients have to be instructed to drink sufficient liquid. Renal function should be measured after the start of concomitant therapy, and periodically thereafter.

The concomitant administration of ibuprofen and ACE-inhibitors may lead to hyperkalaemia.

Potassium sparing diuretics

Concomitant use may cause hyperkalaemia (checking of serum potassium is recommended).

Captopril

Experimental studies indicate that ibuprofen counteracts the effect of captopril of increased sodium excretion.

Corticosteroids

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

Anti-platelet agents (e.g., clopidogrel and ticlopidine) and selective serotonin reuptake inhibitors (SSRIs)

Increased risk of gastrointestinal bleeding (see section 4.4). NSAIDs should not be combined with ticlopidine due to the risk of an additive effect in the inhibition of platelet function.

Methotrexate

NSAIDs inhibit the tubular secretion of methotrexate and certain metabolic interactions may occur resulting in decreased clearance of methotrexate. The administration of ibuprofen within 24 hours before or after administration of methotrexate may lead to an elevated concentration of methotrexate and an increase in its toxic effect. Therefore, concomitant use of NSAIDs and high doses of methotrexate should be avoided. Also, the potential risk of interactions in low dose treatment with methotrexate should be considered, especially in patients with impaired renal function. In combined treatment, renal function should be monitored.

Ciclosporin

The risk of a kidney-damage by ciclosporin is increased by the concomitant administration of certain non-steroidal anti-inflammatory drugs. This effect cannot be ruled out for a combination of ciclosporin and ibuprofen either. Anti-coagulants NSAIDs may enhance the effect of anti-coagulants, such as warfarin (see section 4.4). In case of simultaneous treatment, monitoring of the coagulation state is recommended.

Sulphonylureas

NSAIDs can increase the hypoglycaemic effect of Sulphonylureas. In the case of simultaneous treatment, monitoring of blood glucose levels is recommended.

Tacrolimus

Elevated risk of nephrotoxicity. Zidovudine There is evidence of an increased risk of hemarthrosis and haematomas in HIV positive haemophilia patients receiving concurrent treatment with zidovudine and ibuprofen. There may be an increased risk of haematoxicity during concomitant use of zidovudine and NSAIDs.

Probenecid and sulfinpyrazone

Medicinal products that contain probenecid or sulfinpyrazone may delay the excretion of 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.

CYP2C9 Inhibitors

Concomitant administration of ibuprofen with CYP2C9 inhibitors may increase the exposure to ibuprofen (CYP2C9 substrate). In a study with voriconazole and fluconazole (CYP2C9 inhibitors), an increased S(+)-ibuprofen exposure by approximately 80 to 100% has been shown. Reduction of the ibuprofen dose should be considered when potent CYP2C9 inhibitors are administered

concomitantly, particularly when high-dose ibuprofen is administered with either voriconazole or fluconazole.

Mifepristone

If NSAIDs are used within 8-12 days after the mifepristone administration, they may decrease the effect of mifepristone.

Alcohol

The use of ibuprofen in individuals with chronic alcohol consumption (14-20 drinks/week or more) should be avoided due to increased risk of significant GI adverse effects, including bleeding.

Aminoglycosides

NSAIDs may decrease the excretion of aminoglycosides and increase their toxicity.

Herbal extracts

Ginkgo biloba may potentiate the risk of bleeding with NSAIDs.

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 and of 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 (Section 5.3).

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.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors:

- may expose the foetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension)
- renal dysfunction, which may progress to renal failure with oligohydramnios

- may expose the mother and the neonate, at the end of the pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses
- inhibition of uterine contractions resulting in delayed or prolonged labour

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

Breast-feeding Ibuprofen and its metabolites can pass in low concentrations into the breast milk. No harmful effects to infants are known to date, so for short-term treatment with lower doses interruption of breast-feeding would generally not be necessary, however it is recommended to interrupt breast feeding when using higher doses than 1200 mg daily or longer periods due to the potential to inhibit prostaglandin synthesis in the neonate.

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.

4.7 Effects on Ability to Drive and Use Machines

Ibuprofen, in single or short-term use, has no or negligible influence on the ability to drive and use machines. However, the occurrence of relevant undesirable effects such as fatigue and vertigo can impair reactivity, and the ability to drive a vehicle and/or use machines may be reduced. This particularly applies when combined with alcohol.

4.8 Undesirable Effects

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation, or GI bleeding, sometimes fatal, particularly in the elderly may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following administration. Less frequently, gastritis has been observed. Particularly the risk of gastrointestinal bleeding occurring is dependent on the dose range and the duration of use.

Very rarely have been reported severe hypersensitivity reactions (including infusion site reactions, anaphylactic shock) and serious cutaneous adverse reactions such as bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell's syndrome), erythema multiforme and alopecia.

Exacerbation of infection-related inflammations (e.g., development of necrotising fasciitis) coinciding with the use of non-steroidal anti-inflammatory drugs has been described. This is possibly associated with the mechanism of action of the non-steroidal anti-inflammatory drugs.

Photosensitivity, allergic vasculitis and, in exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection (see section 4.4).

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).

Tabulated summary of adverse reactions

Adverse events are listed below by system organ class and frequency. The following adverse reactions have been reported in post-marketing experience.

Term	**Frequency of occurrence**
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)
Not known	(Cannot be estimated from the available data)

System Organ Class	**Frequency**	**Undesirable effects**
Infections and infestations	Very rare	Exacerbation of infection-related inflammations (e.g., development necrotising fasciitis) coinciding with the use of non-steroidal anti-inflammatory drugs has been described. This is possibly associated with the mechanism of action of the non-steroidal anti-inflammatory drugs.
Blood and lymphatic system disorders	Very rare	Disturbances to blood formation (anaemia, agranulocytosis, leucopoenia, thrombocytopenia, and pancytopenia,). First symptoms are: fever, sore throat, superficial mouth wounds, influenza-like complaints, severe lassitude, nosebleeds, and skin bleeding.
Immune system disorders	Uncommon	Hypersensitivity reactions with skin rashes and itching, as well as asthma attacks (possibly with drop in blood pressure)
	Very rare	Systemic lupus erythematosus, severe hypersensitivity reactions, (face oedema, swelling of the tongue, swelling of the internal larynx with constriction of the airways, difficulty breathing, palpitations, hypotension, and life-threatening shock).
Psychiatric disorders	Uncommon	Anxiety, restlessness
	Rare	Psychotic reactions, nervousness, irritability, confusion or disorientation and depression
Nervous system disorders	Very common	Fatigue or sleeplessness, headache, dizziness

	Uncommon	Insomnia, agitation, irritability, or tiredness
	Very rare	Aseptic meningitis (stiff neck, headache, nausea, vomiting, fever, or confusion). Patients with autoimmune disorders (SLE, mixed connective-tissue disease) appear to be predisposed.
Eye disorders	Uncommon	Visual disturbances
	Rare	Reversible toxic amblyopia
Ear and labyrinth disorders	Common	Vertigo
	Uncommon	Tinnitus
	Rare	Hearing disorders
Cardiac disorders	Very rare	Palpitations, heart failure, myocardial infarction
Vascular disorders	Very rare	Arterial hypertension
Respiratory, thoracic, and mediastinal disorders	Very rare	Asthma, bronchospasm, dyspnoea, and wheezing
Gastrointestinal disorders	Very common	Pyrosis, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation, and slight gastro-intestinal blood losses that may cause anaemia in exceptional cases
	Common	Gastrointestinal ulcers, potentially with bleeding and perforation. Ulcerative stomatitis, exacerbation of colitis and Crohn's disease.
	Uncommon	Gastritis
	Rare	Oesophageal stenosis, exacerbation of diverticular disease, unspecified haemorrhagic colitis. If gastrointestinal bleeding occurs could cause anaemia and haematemesis
	Very rare	Oesophagitis, pancreatitis, formation of intestinal, diaphragm-like strictures
Hepatobiliary disorders	Rare	Jaundice, hepatic dysfunction, hepatic damage, particularly in long-term therapy, acute hepatitis
	Not known	Hepatic insufficiency
Skin and subcutaneous tissue disorders	Common	Skin eruption
	Uncommon	Urticaria, pruritus, purpura (including allergic purpura), skin rash
	Very rare	Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell´s syndrome), erythema multiforme alopecia. Photosensitivity reactions and allergic vasculitis. In exceptional cases, severe skin infections and soft tissues complications in varicella infection (see also 'Infections and infestations')
	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) Acute generalised exanthematous pustulosis (AGEP)
Musculoskeletal and connective tissue disorders	Rare	Stiff neck
Renal and urinary	Uncommon	Reduced urinary excretion and formation of

disorders		oedemas, particularly in patients with arterial hypertension or renal insufficiency, nephrotic syndrome, interstitial nephritis that may be accompanied by acute renal insufficiency.
	Rare	Renal tissue damage (papillary necrosis), particularly in long-term therapy, increased serum uric acid concentration in the blood
General disorders and administration site conditions	Common	Pain and burning sensation in the administration site
	Not known	Injection site reactions such as swelling, haematoma or bleeding.

Health care professionals are asked to report any suspected adverse reactions via the https://pv.pharmacyboardkenya.org

4.9 Overdose

Symptoms Central nervous system disturbances include headache, confusion, nystagmus, tinnitus, dizziness, light-headedness, unconsciousness, convulsions (mainly in children) and ataxia, as well as abdominal pain, nausea, and vomiting, may occur as symptoms of an overdose. In addition, gastrointestinal bleeding, as well as functional disturbances of the liver and kidneys, is possible. There may furthermore be hypotension, hyperkalaemia, hypothermia, respiratory depression, and cyanosis.

In serious poisoning, metabolic acidosis may occur.

Treatment

Treatment is symptomatic and there is no specific antidote. The therapeutic possibilities for treatment of intoxication are dictated by the extent, level, and clinical symptoms according to the common intensive care practices.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids. Propionic acid derivatives. Ibuprofen ATC code: M01AE01 Ibuprofen is a non-steroidal anti-inflammatory drug that, in conventional animal-experiment inflammation models, has proven to be effective, probably through prostaglandin synthesis inhibition. In humans, ibuprofen has an antipyretic effect, reduces inflammatory-related pain and swelling. Furthermore, ibuprofen reversibly inhibits ADP- and collagen- induced platelet aggregation. Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400mg were taken within 8h before or within 30min after immediate release 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 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

Absorption

Ibuprofen Infusion is administered intravenously, therefore there is no absorption process and bioavailability of ibuprofen is 100%. After intravenous administration of ibuprofen in humans, the maximum concentration (Cmax) of S- enantiomer (active) and R-enantiomer is reached at approximately 40minutes, with a rate of infusion of 30minutes.

Distribution

The estimated volume of distribution is 0.11 to 0.21 L/Kg. Ibuprofen is extensively bound to plasma proteins, primarily albumin.

Biotransformation

Ibuprofen is metabolised in the liver into two inactive metabolites, and these together with unmetabolized ibuprofen, are excreted by the kidney either as such or as conjugates.

After an oral application, ibuprofen is already partly absorbed in the stomach and then completely in the small intestine. Following hepatic metabolization (hydroxylation, carboxylation), the pharmacologically inactive metabolites are completely eliminated, mainly renally (90%), but also with the bile.

Elimination

Excretion by the kidney is rapid and complete. The elimination half-life is about 2 hours.

Linearity / non-linearity

Ibuprofen shows linearity in the area under the curve of plasma concentration-time after a single administration of ibuprofen (in a range of 200- 800mg).

Pharmacokinetic / pharmacodynamic relationship(s)

There is a correlation between plasma levels of ibuprofen, its pharmacodynamic properties and overall safety profile. Ibuprofen pharmacokinetics is stereoselective after intravenous and oral administration. The mechanism of action and pharmacology of intravenous ibuprofen do not differ from the mechanism of oral ibuprofen.

Renal impairment

For patients with mild renal impairment, increased unbound (S)-ibuprofen, higher AUC values for (S)-ibuprofen and increased enantiomeric AUC (S/R) ratios have been reported compared with healthy controls.

In end-stage renal disease patients receiving dialysis the mean free fraction of ibuprofen was about 3% compared with about 1% in healthy volunteers. Severe impairment of renal function may result in accumulation of ibuprofen metabolites. The significance of this effect is unknown. The metabolites can be removed by haemodialysis (see sections 4.3 and 4.4).

Hepatic impairment

In cirrhotic patients with moderate hepatic impairment (Child Pugh's score 6-10) treated with racemic ibuprofen an average 2-fold prolongation of the half-life was observed and the enantiomeric AUC ratio (S/R) was significantly lower compared to healthy controls, suggesting an impairment of metabolic inversion of (R)-ibuprofen to the active (S)-enantiomer (see sections 4.3 and 4.4).

5.3 Preclinical Safety Data

The sub chronic and chronic toxicity of ibuprofen in animal trials showed up mainly in the form of lesions and ulcers in the gastrointestinal tract. In vitro and in vivo studies gave no clinically relevant evidence of the mutagenic potential of ibuprofen. In studies in rats and mice no evidence of carcinogenic effects of Ibuprofen was found.

Ibuprofen led to an inhibition of ovulation in rabbits and impaired implantation in various animal species (rabbit, rat, mouse). Experimental studies in rats and rabbits have shown that ibuprofen crosses the placenta. Following the administration of maternal-toxic doses, an increased incidence of malformations (ventricular septal defects) occurred in the offspring of rats.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Disodium phosphate dihydrate, Sodium chloride, Water for Injections, Hydrochloric Acid and Sodium Hydroxide (for pH adjustment).

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf Life

Shelf life 2 years

6.4 Special Precautions for Storage

Do not store above 30°C. From a microbiological point of view, the product should be used immediately after first opening.

Store below 30°C.

6.5 Nature and Contents of Container

Bag sizes: 50ml, 100ml and 150ml The bags are composed of polyolefin/polyamide co-extruded plastic. The bags are overwrapped with a protective tri-laminate pouch.

6.6 Special Precautions for Disposal and Other Handling

Discard after single use. Discard any unused portion. Do not reconnect partially used bags.

Do not remove unit from overwrap until ready for use. The inner bag maintains the sterility of the product. Instructions for use

Opening

- Remove the bag from the over pouch just before use.
- Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution, as sterility may be impaired
- Check solution for limpidity and absence of foreign matter. If solution is not clear or contains foreign matter, discard the solution.

Preparation for administration Use sterile material for preparation and administration.

- Suspend container from eyelet support.
- Remove plastic protector from outlet port at bottom of container:
- Use an aseptic method to set up the infusion.

7. MARKETING AUTHORISATION HOLDER

Tasa Pharma Ltd

Unit C1-C3, Kay Complex, Mombasa Road,

Nairobi, Kenya.

8. MARKETING AUTHORISATION NUMBER(S)

H2025/CTD11570/24995

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08.07.2025

10. DATE OF REVISION OF THE TEXT

21.08.2026