SUMMARY OF PRODUCT CHARACTERISTICS

BRUSTAN-N SUSPENSION

(Ibuprofen Oral Suspension USP 100 mg/5 ml)

1. NAME OF THE MEDICINAL PRODUCT

BRUSTAN-N SUSPENSION

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

BRUSTAN-N SUSPENSION

Each 5 ml contains:
Ibuprofen USP……100 mg

For the full list of excipients, see **section 6.1.**

3. PHARMACEUTICAL FORM

Oral suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Children aged 3 months to 12 years:
Mild to moderate pain, post-immunisation pyrexia, rheumatic or muscular pain, headache, reduction of fever, sore throat, teething pain, toothache, minor aches and pains, symptoms of cold and influenza.

4.2 Posology and method of administration

Children aged 3 months to 12 years:
Not recommended for children weighing less than 5 kg.

For pain and fever – 20 mg/kg/day in divided doses.

Infants 3-6 months:	2.5 ml three times a day. Do not use for more than 24 hours.
Infants 6-12 months:	2.5 ml three times a day.
Children 1-2 years:	2.5 ml three to four times a day
Children 3-7 years:	5 ml three to four times a day
Children 8-12 years:	10 ml three to four times a day

Doses should be taken every 6 – 8 hours when required, and at least 4 hours should be left between doses.

Post-immunisation fever:
2.5 ml (50 mg) followed by one further dose of 2.5 ml (50 mg) six hours later if necessary. No more than 2 doses in 24 hours. If fever is not reduced, consult a doctor.

Do not give to children under 3 months of age.

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

For children aged ≥3 months to ≤5 months: if the child's symptoms worsen or if the symptoms persist for more than 24 hours, consult a doctor.

For children aged 6 months and over: if symptoms worsen or if the symptoms persist for more than 3 days, consult a doctor.

Method of administration
To be taken orally

4.3 Contraindications

- Hypersensitivity to ibuprofen or to 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 heart failure (NYHA Class IV), renal failure or hepatic failure (see **section 4.4**).
- Last trimester of pregnancy (See **section 4.6**)

4.4 Special warnings and precautions for use

Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to relieve 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.

Masking of symptoms of underlying infections:
This medicine 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 reported in bacterial community acquired pneumonia and bacterial complications to varicella. When this medicine is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In nonhospital settings, the patient should consult a doctor if symptoms persist or worsen.

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 cyclooxygenase-2 selective inhibitors should be avoided (see **section 4.5**).

SLE and mixed connective tissue disease:
Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see **Section 4.8**).

Renal:
Renal impairment as renal function may further deteriorate (see **sections 4.3** and **4.8**).

Hepatic:
Hepatic dysfunction (see **sections 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.

Reported 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, reported 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.

Avoid use immediately before or after heart surgery.

Caution should be exercised in patients taking a diuretic.

Impaired female fertility:
Limited evidence reported that drugs which inhibit cyclooxygenase / prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on

withdrawal of treatment. The use of ibuprofen is therefore not recommended in women attempting to conceive.

Gastrointestinal:
NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see **section 4.8**).

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events.

The risk of GI bleeding, ulceration or perforation has been reported to be 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 ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin (see **section 4.5**).

Caution should be taken when using ibuprofen with excessive alcohol or heavy alcohol drinkers. Alcohol may increase the risk of gastrointestinal bleeding.

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

Immune System:
Ibuprofen may cause severe allergic reactions including very rare cases of anaphylaxis (see **section 4.8**). Symptoms may include hives, facial swelling, asthma (wheezing), shock, skin reddening, rash or blisters. If any of these symptoms occur, patients should stop use and seek medical help right away.

Dermatological:
Serious skin reactions, some of them fatal, including exfoliative dermatitis, erythema multiforme, 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 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 skin rash, mucosal lesions or any other sign of hypersensitivity.

Dehydration:
Risk of renal impairment has been reported in dehydrated children.

Do not give this product if your baby or child

- Has (or has had two or more episodes of) a stomach ulcer, perforation or bleeding
- Is allergic to Ibuprofen or any other ingredient of the product, aspirin or other related painkillers
- Is taking other NSAID painkillers, or aspirin with a daily dose above 75 mg
- Speak to a pharmacist or your doctor before giving this product if your baby or child
- Has or has had asthma, diabetes, high cholesterol, high blood pressure, a stroke, heart, liver, kidney or bowel problems, or is dehydrated

If you are an adult taking this product you should not take this product in the last 3 months of pregnancy and you should contact your doctor or pharmacist before taking it in the first 6 months of pregnancy, if trying to get pregnant, if you are elderly or if you are a smoker.

Do not give to babies aged from 3 to under 6 months for more than 24 hours.

Do not give to children aged 6 months and older for more than 3 days.

If symptoms persist or worsen, consult your doctor promptly.

Do not exceed the stated dose.

Not recommended for children under 3 months.

Excipients
Brustan N Suspension contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen should be avoided in combination with:
Aspirin / Acetylsalicylic acid: Unless low-dose aspirin (not above 75mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (See **section 4.4**).

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

Reported 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 reported 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 has been 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:
Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (see **section 4.4**).

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

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

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see **section 4.4**).

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Lithium: There is reported evidence for potential increases in plasma levels of lithium.

Methotrexate: There is 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 reported evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Quinolone antibiotics: Reported 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
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Reported 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 has been reported to be increased from less than 1%, up to approximately

1.5%. The risk has been believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been reported 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. During the first and second trimester of pregnancy, this medicine should not be given unless clearly necessary. If this medicine 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 oligo-hydroamniosis;
- the mother and the neonate, at the end of 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, this medicine has been reported to be contraindicated during the third trimester of pregnancy.

Breast-feeding
In limited reported studies, ibuprofen appears in breast milk in very low concentration and is unlikely to affect breast-fed infants adversely.

Fertility
See **section 4.4** regarding female fertility.

4.7 Effects on ability to drive and use machines

None expected at recommended doses and duration of therapy.

4.8 Undesirable effects

Hypersensitivity reactions have been reported and these may consist of:
a) non-specific allergic reactions and anaphylaxis,
b) respiratory tract reactivity e.g. asthma, aggravated asthma, bronchospasm or dyspnoea,
c) various skin reactions, e.g. pruritus, urticaria, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

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

The adverse drug reactions (ADRs) reported in patients treated with ibuprofen are listed below by System Organ Class. Frequencies are defined in accordance with current guidance 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), not known frequency (cannot be estimated from the available data).

ADRs are presented by frequency category based on 1) incidence in adequately designed reported clinical trials or reported epidemiology studies, when available, or 2) when incidence is unavailable, frequency category is listed as 'Not Known'.

System Organ Class	**Incidence**	**Adverse Drug Reaction**
Blood & 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	Uncommon	Hypersensitivity reactions with urticaria and pruritus
	Very rare	Severe hypersensitivity reactions: Symptoms could be facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema, or severe shock)
	Very rare	Exacerbation of asthma and Bronchospasm
	Not known	In patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease) during treatment with Ibuprofen, single cases of symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been reported (see **section 4.4**)
Nervous system disorders	Uncommon	Headache
	Very rare	Aseptic meningitis – single cases have been reported very rarely.
	Not known	Stroke*
Cardiac disorders	Not known	Oedema, Hypertension and Cardiac failure have been reported in association with NSAID treatment
	Not known	Myocardial infarction*
Gastrointestinal disorders	Uncommon	Abdominal pain
	Uncommon	Dyspepsia
	Uncommon	Nausea
	Rare	Constipation
	Rare	Diarrhoea
	Rare	Flatulence
	Rare	Gastrointestinal ulcer haemorrhage
	Rare	Vomiting
	Very rare	Exacerbation of Colitis and Crohn's disease (see **section 4.4**)
	Very rare	Gastritis
	Very rare	Gastrointestinal haemorrhage, Melaena, Haematemesis, sometimes fatal, particularly in the

		elderly
	Very rare	Peptic ulcer
	Very rare	Perforation
	Very rare	Ulcerative stomatitis
Hepatobiliary disorders	Very rare	Liver disorders
Skin and subcutaneous tissue disorders	Uncommon	Various skin rashes
	Very rare	Severe forms of skin reactions such as bullous reactions, including Stevens-Johnson Syndrome, Erythema multiforme and Toxic Epidermal Necrolysis can occur
	Not known	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome)
	Not known	Acute Generalised Exanthematous Pustulosis (AGEP)
	Not known	Photosensitivity reactions
Renal and urinary disorders	Very rare	Acute Renal failure
	Very rare	Papillary necrosis especially in long term use, associated with increased serum urea and oedema
	Not known	Renal impairment

*Reported 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**).

4.9 Overdose

In children, ingestion of more than 400 mg/kg may cause symptoms. In adults the dose response effect has been reported to be less clear-cut. The half-life in overdose has been reported to be 1.5 –3 hours.

Symptoms

Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, abdominal pain or more rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity has been reported in the central nervous system, manifesting as lethargy and drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions.

In serious poisoning metabolic acidosis may occur and the prothrombin time/ INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur. Exacerbation of asthma has been reported to be possible in asthmatics. Rhabdomyolysis, hypothermia and apnoea (primarily in children) may also rarely occur. Cardiovascular toxicity, including hypotension, cardiac arrhythmias, including ST-segment and T-wave changes, have been reported; ventricular tachycardia/ventricular fibrillation cardiac arrest, and prolonged QTc reported in fatal cases.

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

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids; propionic acid derivative

ATC Code: M01AE01

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

Reported experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some reported pharmacodynamic studies show that when single doses of ibuprofen 400 mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these reported 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 Pharmacokinetics properties

Ibuprofen has been reported to be rapidly absorbed from the gastro-intestinal tract and rapidly distributed throughout the whole body. Peak plasma concentrations occur about 1 to 2 hours after ingestion with food or in 45 minutes if taken on an empty stomach. These times may vary with different dosage forms.

The excretion has been reported to be rapid and complete via the kidneys.

The elimination half-life has been reported to be about 2 hours.

It has been reported to be metabolized to two inactive metabolites and these are rapidly excreted in urine. About 1 percent has been reported to be excreted in urine as unchanged Ibuprofen and about 14 percent as conjugated Ibuprofen.

Ibuprofen has been reported to be extensively bound to plasma proteins.

In limited reported 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

Acesulfame potassium, sodium benzoate, glycerine, sucrose, instant clearjel, xanthan gum, polysorbate 80, quinoline yellow supra, allura red AC, lychee flavour, bubble gum flavour, citric acid, sodium citrate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Do not store above 30°C.
Keep out of the sight and reach of children.

6.5 Nature and contents of container

100 ml amber color glass bottle with ROPP cap packed in a carton along with pack insert

6.6 Special precautions for disposal and other handling

Shake well before use. Return any leftover medicine to the Pharmacist.

7. MARKETING AUTHORISATION HOLDER

Ranbaxy Nigeria Limited

8. MARKETING AUTHORISATION NUMBER(S)

A4-0488

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29-Jun-2007

10. DATE OF REVISION OF THE TEXT

September 2023

REFERENCES

- Summary of Product Characteristics of Calprofen 100 mg/5 ml Oral Suspension (Ibuprofen), McNeil Products Limited, UK, April 2021.