

## Summary of Product Characteristics

### BRUSTAN-N TABLETS

(Ibuprofen Tablets 400 mg)

#### 1. NAME OF THE MEDICINAL PRODUCT

Brustan-N Tablets

#### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

Ibuprofen BP .....400 mg

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

#### 3. PHARMACEUTICAL FORM

Film-coated Tablet

#### 4. CLINICAL PARTICULARS<sup>1</sup>

##### 4.1 Therapeutic indications

**Brustan-N** are indicated for its analgesic and anti-inflammatory effects in the treatment of rheumatoid arthritis (including juvenile rheumatoid arthritis or Still's disease), ankylosing spondylitis, osteoarthritis and other non-rheumatoid (seronegative) arthropathies.

In the treatment of non-articular rheumatic conditions, Brustan-N are indicated in periarticular conditions such as frozen shoulder (capsulitis), bursitis, tendonitis, tenosynovitis and low back pain; Brustan-N can also be used in soft tissue injuries such as sprains and strains.

**Brustan-N** are also indicated for its analgesic effect in the relief of mild to moderate pain such as dysmenorrhoea, dental and post-operative pain and for symptomatic relief of headache, including migraine headache.

##### 4.2 Posology and method of administration

**Brustan-N** (Ibuprofen 400 mg tablets) may not be suitable for all dosages and therefore, other suitable available strengths and/or dosage forms of ibuprofen should be used in such cases.

Section 4.8 may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

*Adults and children over 12 years of age:* The recommended dosage of ibuprofen is 1200-1800 mg daily in divided doses. Some patients can be maintained on 600-1200 mg daily. In severe or acute conditions, it can be advantageous to increase the dosage until the acute phase is brought under control, provided that the total daily dose does not exceed 2400 mg in divided doses.

**Brustan-N** are not recommended for children weighing less than 7 kg.

## **4.2 Special populations**

### ***Elderly***

The elderly are at increased risk of serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy. If renal or hepatic function is impaired, dosage should be assessed individually.

### ***Renal impairment***

Patients with mild to moderate renal impairment, (see section 4.4) and patients with severe renal insufficiency (see section 4.3).

### ***Hepatic impairment***

Patients with mild to moderate hepatic impairment, (see section 4.4) and patients with severe hepatic dysfunction (see section 4.3).

For oral administration. It is recommended that patients with sensitive stomachs take ibuprofen with food. If taken shortly after eating, the onset of action of ibuprofen may be delayed. To be taken preferably with or after food, with plenty of fluid. Ibuprofen tablets should be swallowed whole and not chewed, broken, crushed or sucked on to avoid oral discomfort and throat irritation.

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

### ***Pediatric population***

The daily dosage of ibuprofen is 20 mg/kg of body weight in divided doses.

For young children, more suitable formulations are available and should be considered.

In Juvenile Rheumatoid Arthritis, up to 40 mg/kg of body weight daily in divided doses may be taken.

### **Method of administration**

**Brustan-N** tablets are for oral administration. It is recommended that patients with sensitive stomachs take ibuprofen with food. If taken shortly after eating, the onset of action of ibuprofen may be delayed. To be taken preferably with or after food, with plenty of fluid.

**Brustan-N** tablets should be swallowed whole and not chewed, broken, crushed or sucked on to avoid oral discomfort and throat irritation..

### **4.3 Contraindications**

**Brustan-N Tablets** are contraindicated

- In patients with hypersensitivity to the active substance or to any of the excipients.
- In patients who have previously shown hypersensitivity reactions (e.g. asthma, urticaria, angioedema or rhinitis) after taking ibuprofen, aspirin or other NSAIDs.
- Also contraindicated in patients with a history of gastrointestinal bleeding or perforation, related to previous NSAID therapy. Ibuprofen should not be used in patients with active, or history of, recurrent peptic ulcer or gastrointestinal haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- In patients with conditions involving an increased tendency to bleeding.
- In patients with severe heart failure (NYHA Class IV), hepatic failure and renal failure (see section 4.4).
- During the 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 section 4.2).

**Brustan-N** tablet contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medication.

As with other NSAIDs, ibuprofen may mask the signs of infection.

The use of ibuprofen with concomitant NSAIDs, including cyclooxygenase-2 selective inhibitors, should be avoided due to the increased risk of ulceration or bleeding (see section 4.5).

The diagnosis of medication overuse headache (MOH) should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of analgesic medication. Patients with medication overuse headache should not be treated by increasing the dose of the analgesic. In such cases the use of analgesics should be discontinued.

The concomitant consumption of excessive alcohol with NSAIDs, including ibuprofen may increase the risk of adverse effects on the gastrointestinal tract, such as GI haemorrhage or the central nervous system, possibly due to an additive effect.

#### *Elderly*

The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation, which may be fatal (see section 4.2).

#### *Paediatric population*

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

#### *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 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 aspirin, or other drugs likely to increase gastrointestinal risk (see below and section 4.5).

Patients with a history of gastrointestinal disease, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal 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).

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

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

### *Respiratory disorders and hypersensitivity reactions*

Caution is required if ibuprofen 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 precipitate bronchospasm, urticaria or angioedema in such patients.

### *Cardiac, renal and hepatic impairment*

The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. The habitual concomitant intake of various similar painkillers further increases this risk. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. For these patients, use the lowest effective dose, for the shortest possible duration and monitor renal function especially in long-term treated patients (see section 4.3).

Ibuprofen should be given with care to patients with a history of heart failure or hypertension since oedema has been reported in association with ibuprofen administration.

### *Cardiovascular and cerebrovascular effects*

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical studies have reported that use of ibuprofen, particularly at a high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events such as myocardial infarction or stroke. Overall, epidemiological studies reported, do not suggest that low dose ibuprofen (e.g.  $\leq 1200\text{mg/day}$ ) 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 (2400mg/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 (2400mg/day) are required.

### *Renal effects*

Caution should be used when initiating treatment with ibuprofen in patients with considerable dehydration.

As with other NSAIDs, long-term administration of ibuprofen has resulted in renal papillary necrosis and other renal pathologic changes. Renal toxicity has also been reported in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependant

reduction in prostaglandin formation and, secondarily, in renal blood flow, which may cause renal failure. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pre-treatment state.

#### *SLE and mixed connective tissue disease*

In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see section 4.8).

#### *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 of these reactions early in the course of therapy, the onset of the reaction occurring within the first month of treatment in the majority of cases. Ibuprofen should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

In exceptional cases, varicella can be at the origin of 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.

#### *Haematological effects*

Ibuprofen, like other NSAIDs, can interfere with platelet aggregation and prolong bleeding time in normal subjects.

#### *Aseptic meningitis*

Aseptic meningitis has been reported on rare occasions in patients on ibuprofen therapy. Although it is probably more likely to occur in patients with systemic lupus erythematosus and related connective tissue diseases, it has been reported in patients who do not have an underlying chronic disease.

#### *Impaired female fertility*

The use of ibuprofen may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of ibuprofen should be considered.

### **4.5 Interaction with other medicinal products and other forms of interaction**

Care should be taken in patients treated with any of the following drugs as interactions have been reported in some patients.

*Antihypertensives, beta-blockers and diuretics:* NSAIDs may reduce the effect of anti-hypertensives, such as ACE inhibitors, angiotensin-II receptor antagonists, beta-blockers and diuretics. Diuretics can also increase the risk of nephrotoxicity of NSAIDs.

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

*Cholestyramine:* The concomitant administration of ibuprofen and cholestyramine may reduce the absorption of ibuprofen in the gastrointestinal tract. However, the clinical significance is unknown.

*Lithium:* Decreased elimination of lithium.

*Methotrexate:* NSAIDs may inhibit the tubular secretion of methotrexate and reduce clearance of methotrexate.

*Cyclosporin:* Increased risk of nephrotoxicity.

*Mifepristone:* A decrease in the efficacy of the medicinal product can theoretically occur due to the antiprostaglandin properties of NSAIDs. Limited evidence suggests that coadministration of NSAIDs on the day of prostaglandin administration does not adversely influence the effects of mifepristone or the prostaglandin on cervical ripening or uterine contractility and does not reduce the clinical efficacy of medicinal termination of pregnancy.

*Other analgesics and cyclooxygenase-2 selective inhibitors:* Avoid concomitant use of two or more NSAIDs, including Cox-2 inhibitors, as this may increase the risk of adverse effects (see section 4.4).

*Aspirin (Acetylsalicylic acid):* As with other products containing NSAIDs, concomitant administration of ibuprofen and aspirin 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 aspirin 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 use (see section 5).  
*Corticosteroids:* Increased risk of gastrointestinal ulceration or bleeding with NSAIDs (see section 4.4).

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

*Anticoagulants:* NSAIDs may enhance the effects of anticoagulants, such as warfarin (see section 4.4).

*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.

*Sulfonylureas:* NSAIDs may potentiate the effects of sulfonylurea medications. There have been rare reports of hypoglycaemia in patients on sulfonylurea medications receiving ibuprofen.

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

*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.

*Aminoglycosides:* NSAIDs may decrease the excretion of aminoglycosides.

*Herbal extracts:* *Ginkgo biloba* may potentiate the risk of bleeding with NSAIDs.

*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.

## **4.6 Fertility, pregnancy and lactation**

### **Pregnancy**

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo/foetal development. Data reported from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after the use of a prostaglandin synthesis inhibitor in early pregnancy. The risk is believed to increase with dose and duration of therapy. In animals, the administration of a prostaglandin synthesis inhibitor has been reported to result in increased pre- and post-implantation losses 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, ibuprofen should not be given unless clearly necessary. If ibuprofen is used by a woman attempting to conceive, or during the first or 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 the following:

- Cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension)
- Renal dysfunction, which may progress to renal failure with oligohydramnios.

At the end of pregnancy, prostaglandin synthesis inhibitors may expose the mother and the neonate to the following:

- Possible prolongation of bleeding time
- Inhibition of uterine contractions, which may result in delayed or prolonged labour.

Consequently, ibuprofen is contraindicated during the third trimester of pregnancy.

### **Lactation**

In the limited studies reported so far, NSAIDs can appear in the breast milk in very low concentrations. NSAIDs should, if possible, be avoided when breastfeeding.

### **Fertility**

The use of ibuprofen may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of ibuprofen should be considered.

### **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**

*Gastrointestinal disorders:* The most commonly reported 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, gastrointestinal haemorrhage and exacerbation of colitis and Crohn's disease (see section 4.4) have been

reported following ibuprofen administration. Less frequently, gastritis, duodenal ulcer, gastric ulcer and gastrointestinal perforation have been reported.

*Immune system disorders:* Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, very rarely, erythema multiforme, bullous dermatoses (including Stevens- Johnson syndrome and toxic epidermal necrolysis).

*Cardiac disorders and vascular disorders:* Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment. Reported clinical studies suggest that use of ibuprofen, particularly at high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events such as myocardial infarction or stroke (see section 4.4).

*Infections and infestations:* Rhinitis and aseptic meningitis (especially in patients with existing autoimmune disorders, such as systemic lupus erythematosus and mixed connective tissue disease) with symptoms of stiff neck, headache, nausea, vomiting, fever or disorientation (see section 4.4).

Exacerbation of infection-related inflammations coinciding with the use of NSAIDs has been reported. If signs of an infection occur or get worse during use of Ibuprofen the patient is therefore recommended to go to a doctor without delay.

*Skin and subcutaneous tissue disorders:* In exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection (see also "Infections and infestations")

The following adverse reactions possibly related to ibuprofen are reported. Frequency groupings are classified according to the subsequent conventions: very common ( $\geq 1/10$ ), Common ( $\geq 1/100$  to  $< 1/10$ ), Uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), Rare ( $\geq 1/10,000$  to  $< 1/1,000$ ), Very rare ( $< 1/10,000$ ) and Not known (cannot be estimated from the available reported data).

<b>System organ class</b>	<b>Frequency</b>	<b>Adverse reaction</b>
Infections and infestations	Uncommon	Rhinitis
	Rare	Meningitis aseptic (see section 4.4)
Blood and lymphatic system disorders	Rare	Leukopenia, thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia, haemolytic anaemia
Immune system disorders	Uncommon	Hypersensitivity
	Rare	Anaphylactic reaction
Psychiatric disorders	Uncommon	Insomnia, anxiety

<b>System organ class</b>	<b>Frequency</b>	<b>Adverse reaction</b>
	Rare	Depression, confusional state
Nervous system disorders	Common	Headache, dizziness
	Uncommon	Paraesthesia, somnolence
	Rare	Optic neuritis
Eye disorders	Uncommon	Visual impairment
	Rare	Toxic optic neuropathy
Ear and labyrinth disorders	Uncommon	Hearing impaired , tinnitus, vertigo
Respiratory, thoracic and mediastinal disorders	Uncommon	Asthma, bronchospasm, dyspnoea
Gastrointestinal disorders	Common	Dyspepsia, diarrhoea, nausea, vomiting, abdominal pain, flatulence, constipation, melaena, haematemesis, gastrointestinal haemorrhage
	Uncommon	Gastritis, duodenal ulcer, gastric ulcer, mouth ulceration, gastrointestinal perforation
	Very rare	Pancreatitis
	Not known	Exacerbation of Colitis and Crohn's disease
Hepatobiliary disorders	Uncommon	Hepatitis, jaundice, hepatic function abnormal
	Very Rare	Hepatic failure
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria, pruritus, purpura, angioedema, photosensitivity reaction
	Very rare	Severe forms of skin reactions (e.g. Erythema multiforme, bullous reactions, including Stevens-Johnson syndrome, and toxic epidermal necrolysis)
Renal and urinary disorders	Uncommon	Nephrotoxicity in various forms e.g. Tubulointerstitial nephritis, nephrotic syndrome and renal failure
General disorders and administration site conditions	Common	Fatigue
	Rare	Oedema
Cardiac disorders	Very rare	Cardiac failure, myocardial infarction (also see section 4.4)
Vascular disorders	Very rare	Hypertension

## 4.9 Overdose

### *Toxicity*

Signs and symptoms of toxicity have generally not been reported at doses below 100 mg/kg in children or adults. However, supportive care may be needed in some cases. Children have been reported to manifest signs and symptoms of toxicity after ingestion of 400 mg/kg or greater.

### *Symptoms*

Most patients who have ingested significant amounts of ibuprofen will manifest symptoms within 4 to 6 hours. The most frequently reported symptoms of overdose include nausea, vomiting, abdominal pain, lethargy and drowsiness. Central nervous system (CNS) effects include headache, tinnitus, dizziness, convulsion, and loss of consciousness. Nystagmus, metabolic acidosis, hypothermia, renal effects, gastrointestinal bleeding, coma, apnoea, diarrhoea and depression of the CNS and respiratory system have also been rarely reported. In serious poisoning metabolic acidosis may occur. Disorientation, excitation, fainting and cardiovascular toxicity, including hypotension, bradycardia and tachycardia have been reported. In cases of significant overdose, renal failure and liver damage are possible. Large overdoses are generally well tolerated when no other drugs are being taken.

### *Therapeutic measures*

Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.

Good urine output should be ensured.

Renal and liver function should be closely monitored.

Patients should be observed for at least four hours after ingestion of potentially toxic amounts.

Frequent or prolonged convulsions should be treated with intravenous diazepam. Other measures may be indicated by the patient's clinical condition

## **5. PHARMACOLOGICAL PROPERTIES<sup>1</sup>**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic classification: Anti-inflammatory and antirheumatic products, nonsteroidal; propionic acid derivatives.

ATC code: M01AE01

- **Mechanism of action**

Ibuprofen is a propionic acid derivative with analgesic, anti-inflammatory and anti-pyretic activity. The drug's therapeutic effects as an NSAID are thought to result from its inhibitory effect on the enzyme cyclo-oxygenase, which results in a marked reduction in prostaglandin synthesis.

Reported experimental data suggests that ibuprofen may competitively inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies report that when single doses of ibuprofen 400mg were 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 reported. 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).

- **Pharmacokinetics**

Ibuprofen is rapidly absorbed from the gastrointestinal tract, peak serum concentrations occurring 1-2 hours after administration. The elimination half-life is approximately 2 hours.

Ibuprofen is metabolised in the liver to two inactive metabolites and these, together with unchanged ibuprofen, are excreted by the kidney either as such or as conjugates. Excretion by the kidney is both rapid and complete.

Ibuprofen is extensively bound to plasma proteins.

### **5.3 Preclinical safety data**

There are no preclinical data of relevance which are additional to that already included.

## **6. PHARMACEUTICAL PARTICULARS**

## **6.1 List of excipients**

– *List of inactive ingredients:* Maize Starch; Calcium Hydrogen Phosphate (dehydrate); Microcrystalline Cellulose (PH101); Tartazine Lake CI No. 19140; Sunset Yellow Lake CI15985 (regular); Purified Water; Gelatin.

*Extragranular ingredients:* Purified talc; Colloidal Anhydrous Silic; Maize Starch.

*Film Coating Ingredients:* Hypermellose; Macrogol 400; Titanium Dioxide; Tartazine Lake CI No. 19140

## **6.2 Incompatibilities**

Not applicable.

## **6.3 Shelf life**

36 months

## **6.4 Special precautions for storage**

Do not store above 30oC.

## **6.5 Nature and contents of container**

PVC blister Pack

## **6.6 Special precautions for disposal and other handling**

Not Applicable

## **7. Marketing authorisation holder**

Ranbaxy Nigeria Limited

## **8. Marketing authorisation number**

NAFDAC Reg. No.: 04-0694

## **9. Date of first authorisation/renewal of the authorisation**

27/08/1996

## **10. Date of revision of the text**

August 2023

## **Reference**

1. Summary of Product Characteristics of **BRUFEN tablets 400mg**, Mylan Products Limited, UK, November 2022.

*Brufen® is the registered trademark of Mylan Products Limited and is not trademark of Sun Pharmaceuticals Industries Limited. The maker of this brand is not affiliated with and does not endorse Sun Pharmaceuticals Industries Limited or its products.*