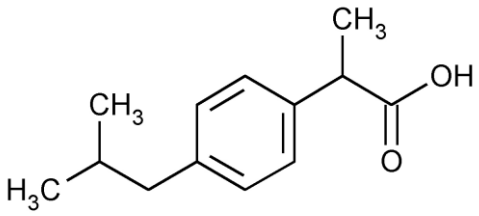
# PRODUCT INFORMATION

# BRUFEN® TABLETS AND SYRUP

## NAME OF THE MEDICINE

Ibuprofen 400 mg tablet; 100 mg/5 mL Syrup

The structural formula for ibuprofen is shown below:




CAS Number: 15687-27-1

## DESCRIPTION

Ibuprofen is a (±)-2-(*p*-isobutylphenyl) propionic acid. Ibuprofen is a white crystalline solid with a melting point of 74 - 77°C and is practically insoluble in water (< 0.1mg/mL) and readily soluble in organic solvents such as ethanol and acetone.

## PHARMACOLOGY

Ibuprofen is a nonsteroidal anti-inflammatory agent that possesses analgesic and antipyretic activities. Its mode of action, like that of other nonsteroidal anti-inflammatory agents, is not completely understood, but may be related to prostaglandin synthetase inhibition.

Ibuprofen has shown anti-inflammatory, analgesic and antipyretic activity in both animal and human studies. These properties provide symptomatic relief of inflammation and pain in rheumatoid arthritis, osteoarthritis and allied conditions.

### *Pharmacokinetics*

Absorption: Ibuprofen is well absorbed after oral administration. Single doses of 200 mg taken on an empty stomach by volunteers produced peak serum levels after approximately 45 minutes. When taken after food, absorption was slower, peak levels appearing at 1.5 to 3 hours.

Bioavailability: The bioavailability of ibuprofen from one "Brufen 400 mg" tablet is equivalent to that from two "Brufen 200 mg" tablets, and 20 mL of a 2% Brufen Syrup.

Distribution: Apparent volume of distribution is 0.14 L/kg. Ibuprofen and its metabolites readily cross the placental barrier in pregnant rabbits and rats. It is not known if the drug enters the CSF or is excreted in breast milk.

Protein Binding: 99% of ibuprofen is protein bound. The high protein binding of the drug should be borne in mind when prescribing ibuprofen together with other protein bound drugs which bind to the same site on human serum albumin.

Metabolism: About 90% of ibuprofen is metabolised to two major metabolites (A and B), and these are as follows:

Metabolite A: (+) 2-4'-(2 hydroxy-2-methylpropylphenyl) propionic acid.
Metabolite B: (+) 2-4'-(2-carboxypropylphenyl) propionic acid.

Both metabolites are dextrorotatory and are devoid of anti-inflammatory and analgesic activity.

Normal volunteers and patients with rheumatoid arthritis were given 800 mg ibuprofen as a single dose. After 14-24 hours the plasma levels of drug and metabolites were less than 0.25 micrograms/mL.

Excretion: The kidney is the major route of excretion. 95% of the drug was excreted in the urine within 24 hours of a single dose of 500 mg, 35% as metabolite A (15% free, 20% conjugated); 51% as metabolite B (42% free, 9% conjugated); ibuprofen 9% (1% free, 8% conjugated).

Half-life: Plasma half-life of ibuprofen is in the range 1.9 to 2.2 hours.

## INDICATIONS

Rheumatoid arthritis
Osteoarthritis
Juvenile rheumatoid arthritis
Primary dysmenorrhoea
Pyrexia

Brufen is also indicated for the relief of acute and/or chronic pain states in which there is an inflammatory component.

## CONTRAINDICATIONS

Known hypersensitivity to ibuprofen or any of the inactive ingredients.

Hypersensitivity (e.g. asthma, rhinitis or urticaria) to aspirin or other nonsteroidal anti-inflammatory drugs.

History or active gastrointestinal bleeding or perforation related to previous NSAID therapy.

History or active, ulcerative colitis, Crohn's disease, recurrent peptic ulceration or gastrointestinal haemorrhage (defined as two or more distinct episodes of proven ulceration or bleeding).

Severe heart failure (NYHA IV).

Patients with severe hepatic impairment.

Treatment of perioperative pain in setting of coronary artery bypass surgery (CABG).

Severe renal failure (glomerular filtration below 30 mL/min).

Conditions involving an increased tendency or active bleeding.

During the third trimester of pregnancy.

Pregnancy (see 'Use in Pregnancy').

Lactation (see 'Use in Lactation').

## PRECAUTIONS

### General Precautions

Prolonged use of any painkillers may induce headaches, which must not be treated with increased doses of the painkillers, including ibuprofen.

Through concomitant consumption of alcohol, NSAID-related undesirable effects, particularly those that concern the gastrointestinal tract or the central nervous system, may be increased on use of NSAIDs.

### Cardiovascular Thrombotic Events

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/ day) or increased duration of use, may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Patients with cardiovascular disease, history of atherosclerotic cardiovascular disease or cardiovascular risk factors may also be at greater risk. 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, hyperlipidemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

To minimize the potential risk of an adverse cardiovascular event in patients taking an NSAID, especially in those with cardiovascular risk factors, the lowest effective dose

should be used for the shortest possible duration (see 'DOSAGE AND ADMINISTRATION').

Physicians and patients should remain alert for such CV events, even in the absence of previous CV symptoms. Patients should be informed about signs and/or symptoms of serious CV toxicity and the steps to take if they occur.

There is no consistent evidence that the concurrent use of aspirin mitigates the possible increased risk of serious cardiovascular thrombotic events associated with NSAID use.

**Hypertension**
NSAIDs may lead to onset of new hypertension or worsening of pre-existing hypertension and patients taking antihypertensives with NSAIDs may have an impaired anti-hypertensive response. Caution is advised when prescribing NSAIDs to patients with hypertension. Blood pressure should be monitored closely during initiation of NSAID treatment and at regular intervals thereafter.

**Heart Failure**
Fluid retention and oedema have been observed in some patients taking NSAIDs, therefore caution is advised in patients with fluid retention or heart failure.

**Gastrointestinal Events**
Ibuprofen should be used with extreme caution, and at the lowest effective dose, in patients with a history of gastro-intestinal haemorrhage or ulcer since their condition may be exacerbated.

All NSAIDs can cause gastrointestinal discomfort and serious, potentially fatal gastrointestinal effects such as ulcers, bleeding and perforation which may increase with dose or duration of use, but can occur at anytime without warning. Upper GI ulcers, gross bleeding or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3-6 months and in about 2-4% of patients treated for one year. These trends continue with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short term therapy is not without risk.

Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, as well as patients requiring concomitant low dose aspirin, or for other drugs likely to increase gastrointestinal risk (see 'INTERACTIONS WITH OTHER MEDICINES').

The concomitant administration of ibuprofen and other NSAIDs, including cyclooxygenase-2 (Cox-2) selective inhibitors, should be avoided due to the increased risk of ulceration or bleeding (see 'INTERACTIONS WITH OTHER MEDICINES').

Caution is advised in patients with risk factors for gastrointestinal events who may be at greater risk of developing serious gastrointestinal events, e.g. the elderly, those with a history of serious gastrointestinal events, smoking and alcoholism. When gastrointestinal bleeding or ulcerations occur in patients receiving NSAIDs, the drug

should be withdrawn immediately. Doctors should warn patients about signs and symptoms of serious gastrointestinal toxicity.

Caution should be exercised in patients receiving concomitant medication which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin re-uptake inhibitors or antiplatelet drugs such as aspirin (see 'INTERACTIONS WITH OTHER MEDICINES').

The concurrent use of aspirin and NSAIDs also increases the risk of serious gastrointestinal adverse events.

**Severe Skin Reactions**
NSAIDs may very rarely cause serious cutaneous adverse events such as exfoliative dermatitis, toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS), which can be fatal and occur without warning. These serious adverse events are idiosyncratic and are independent of dose or duration of use. Patients should be advised of the signs and symptoms of serious skin reactions and to consult their doctor at the first appearance of a skin rash or any other sign of hypersensitivity.

Severe skin infections and soft-tissue complications may occur in patients with a varicella infection. The role of NSAIDs in the worsening of these infections is uncertain, therefore it is advisable to avoid the use of ibuprofen in known or suspected cases of varicella.

**Infections and Infestations**
Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of NSAIDs has been described. 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.

**Respiratory Disorders**
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 ibuprofen has been reported to cause bronchospasm, urticarial or angioedema in such patients.

**Ophthalmological Effects**
Adverse ophthalmological effects have been observed with NSAIDs; accordingly, patients who develop visual disturbances during treatment with ibuprofen should have an ophthalmological examination.

**Impaired Liver Function or a History of Liver Disease**
As with other NSAIDs, elevations of one or more liver function tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may resolve with continued therapy. Meaningful elevations (three times the upper limit of normal) of ALT or AST occurred in controlled clinical trials in less than 1% of patients.
Physicians and patients should remain alert for hepatoxicity. Patients should be informed about the signs and/or symptoms of hepatotoxicity (e.g. nausea, fatigue,

lethargy, pruritis, jaundice, abdominal tenderness in the right upper quadrant and "flu-like" symptoms) and the steps to take should these signs and/or symptoms occur. Patients with impaired liver function or a history of liver disease who are on long term ibuprofen therapy should have hepatic function monitored at regular intervals. Ibuprofen has been reported to have a minor and transient effect on liver enzymes.

Severe hepatic reactions, including jaundice and cases of fatal hepatitis, though rare, have been reported with ibuprofen as with other NSAIDs. If abnormal liver tests persist or worsen, or if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g. eosinophilia, rash, etc.), ibuprofen should be discontinued.

**Impaired Renal Function**
Caution should be used when initiating treatment with ibuprofen in patients with considerable dehydration. There is a risk of renal impairment especially in dehydrated children and adolescents.

The two major metabolites of ibuprofen are excreted mainly in the urine and impairment of renal function may result in their accumulation. The significance of this is unknown. NSAIDs have been reported to cause nephrotoxicity in various forms; interstitial nephritis, nephrotic syndrome and renal failure. In patients with renal, cardiac or hepatic impairment, those taking diuretics and ACE Inhibitors, and the elderly, caution is required since the use of NSAIDs may result in deterioration of renal function. The long term concomitant intake of similar analgesics further increases the risk. For patients with renal, hepatic or cardiac impairment, use the lowest effective dose, for the shortest possible duration and monitor renal fuction especially in long term treated patients.

**Combination use of ACE inhibitors or angiotensin receptor antagonists, anti-inflammatory drugs and thiazide diuretics**
The use of an ACE inhibiting drug (ACE-inhibitor or angiotensin receptor antagonist, an anti-inflammatory drug (NSAID or COX-2 inhibitor) and thiazide diuretic at the same time increases the risk of renal impairment. This includes use in fixed-combination products containing more than one class of drug. Combined use of these medications should be accompanied by increased monitoring of serum creatinine, particularly at the institution of the combination. The combination of drugs from these three classes should be used with caution particularly in elderly patients or those with pre-existing renal impairment.

**Aseptic Meningitis**
Aseptic meningitis has been reported only rarely, usually but not always in patients with systemic lupus erythematosus (SLE) or other connective tissue disorders.

**Haematological Monitoring**
Blood dyscrasias have been rarely reported. Patients on long-term therapy with ibuprofen should have regular haematological monitoring.

**Coagulation Defects**
Like other NSAIDs, ibuprofen can inhibit platelet aggregation. Ibuprofen has been shown to prolong bleeding time (but within the normal range), in normal subjects. Because this prolonged bleeding effect may be exaggerated in patients with underlying haemostatic defects, ibuprofen should be used with caution in persons with intrinsic coagulation defects and those on anti-coagulation therapy.

**Masking Signs of Infection**
As with other drugs of this class, ibuprofen may mask the usual signs of infection.

**Special Precautions**
In order to avoid exacerbation of disease or adrenal insufficiency, patients who have been on prolonged corticosteroid therapy should have their therapy tapered slowly rather than discontinued abruptly when ibuprofen is added to the treatment program.

**Use in Pregnancy** (Category C)
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo/foetal development. Data 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 shown 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 labor

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

**Use in Labour and Delivery**
Administration of ibuprofen is not recommended during labour and delivery. The onset of labor may be delayed and the duration increased with a greater bleeding tendency in both mother and child.

**Use in Lactation**
Ibuprofen is not recommended for use in nursing mothers.

**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.

**Interactions with Other Medicines**
Care should be taken in patients treated with anti-coagulants, such as warfarin, due to an enhanced effect of anti-coagulants.

Concurrent use of NSAIDs and warfarin has been associated with severe sometimes fatal haemorrhage. The mechanism of this interaction is not known but may involve increased bleeding from NSAID-induced gastrointestinal ulceration or an additive effect of NSAID inhibition of platelet function with the anticoagulant effect of warfarin.

Brufen should only be used in patients taking warfarin if absolutely necessary. Patients taking this combination must be closely monitored.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding.

Aminoglycosides: NSAIDs may decrease the excretion of aminoglycosides.

Ibuprofen has been shown to decrease the renal clearance and increase plasma concentrations of lithium. Lithium plasma concentrations should be monitored in patients on concurrent ibuprofen therapy.

Ibuprofen like other NSAIDs can reduce the antihypertensive effect of ACE inhibitors, angiotensin II-receptor antagonists and beta-blockers with possible loss of blood pressure control and can attenuate the natriuretic effects of diuretics. Diuretics can also increase the risk of nephrotoxicity of NSAIDs. The combined use of the three classes of drugs, diuretics, an ACE inhibiting drug (ACE-inhibitor or angiotensin receptor antagonist and an anti-inflammatory drug (NSAID or COX-2 inhibitor) all at the same time increases the risk of renal impairment (see 'PRECAUTIONS').

NSAIDs may exacerbate cardiac failure, reduce glomerular filtration rate and increase plasma cardiac glycoside levels. Care should therefore be taken in patients treated with cardiac glycosides.

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

Corticosteroids: Increased risk of gastrointestinal bleeding.

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

Other analgesics: Avoid concomitant use of two or more NSAIDs, including aspirin and cyclooxygenase-2 (COX-2) selective inhibitors, because of the potential of increased adverse effects. Ibuprofen antagonizes the irreversible inhibition of platelet cox-1 induced by low dose aspirin. To reduce this effect, ibuprofen should be administered at least 8 hours before or 30 minutes after taking low dose aspirin.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when a single daily dose of ibuprofen 400mg was given within 8 hours before or within 30 minutes after immediate release aspirin (81mg), and when multiple daily doses of ibuprofen 400mg are given with aspirin, a decreased effect of aspirin on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of this data to the clinical situation the possibility that regular, long term use of ibuprofen may reduce the cardio-protective effect of aspirin cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use.

Ciclosporin or Tacrolimus: Increased risk of nephrotoxicity when used with NSAIDs.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

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 hypoglycemia in patients on sulfonylurea medications receiving ibuprofen.

Zidovudine: Increased risk of hematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of hemarthroses and hematoma in HIV(+) hemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

NSAIDs inhibit tubular secretion of methotrexate in animals. As a result, reduction of clearance of methotrexate may occur. Use of high doses of methotrexate concomitant with NSAIDs should be avoided. At low doses of methotrexate caution should be used if ibuprofen is administered concomitantly.

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.

**Effects on Ability to Drive and To Use Machines**
Following treatment with ibuprofen, the reaction time of patients may be affected. This should be taken into account where increased vigilance is required, e.g. when driving a car or operating machinery.

**Excipients – Film coated tablets**
**Lactose**
This medicine contains lactose monohydrate. Patients with rare hereditary forms of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption syndrome should not take this medicine.

**Excipients – Oral suspension**
**Sucrose and sorbitol**
This medicine contains sucrose and sorbitol. Patients with rare hereditary forms of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine. This should also be taken into account in patients with diabetes mellitus. May be harmful to teeth.

**Methyl hydroxybenzoate and propyl hydroxybenzoate.**
The oral suspension contains methyl hydroxybenzoate and propyl hydroxybenzoate. May cause allergic reactions (possibly delayed).

**Sunset yellow (E110)**
May cause allergic reactions.

**ADVERSE EFFECTS**

**More common reactions: (greater than 1%)**

***Gastrointestinal:*** The most commonly observed adverse events are gastrointestinal in nature. Gastrointestinal complaints include nausea, epigastric pain, heartburn, diarrhoea, abdominal distress, nausea and vomiting, dyspepsia, constipation, abdominal cramps or pain, gastrointestinal haemorrhage, melaena, fullness of the GI tract (bloating and flatulence).

***Auditory and vestibular***: Tinnitus, hearing impaired.

***Cardiovascular***: Oedema, fluid retention; fluid retention generally responds promptly to discontinuation of the drug.

***Central nervous system:*** Dizziness, headache, nervousness.

***Dermatological***: Rash (including maculopapular type), pruritus.

***General:*** Decreased appetite, fatigue.

**Less common reactions: (less than 1%)**

***Central nervous system:*** Depression, insomnia, anxiety, confusion, emotional lability, somnolence, aseptic meningitis with fever and coma.

***Dermatological:*** Vesiculobullous eruptions, urticaria, erythema multiforme, Stevens-Johnson syndrome, alopecia.

***Gastrointestinal:*** Gastric or duodenal ulcer with bleeding and/or perforation, mouth ulceration, pancreatitis, gastritis, hepatitis, jaundice, abnormal liver function tests.

***Haematological:*** Neutropenia, leucopenia, agranulocytosis, aplastic anaemia, haemolytic anaemia (sometimes Coombs positive), thrombocytopenia with or without purpura, eosinophilia and decrease in haemoglobin and haematocrit.

***Cardiovascular:*** Cardiac failure, myocardial infarction (see 'PRECAUTIONS - Cardiovascular Thrombotic Events')

***Vascular disorder:*** Hypertension

***Respiratory, thoracic and mediastinal disorders:*** Asthma, bronchospasm, dyspnoea

**Infections and infestations**: Rhinitis and meningitis aseptic

***Ocular:*** Amblyopia (blurred and/or diminished vision, scotomata and/or changes in colour vision) have occurred but is usually reversed after cessation of therapy. Any patient with eye complaints should have an ophthalmological examination which includes central vision fields (see 'WARNINGS'). Visual impairment and toxic neuropathy have also been reported.

***Allergic:*** Syndrome of abdominal pain, fever, chills, nausea and vomiting, hypersensitivity, anaphylaxis.

**Precise Incidence Unknown (but less than 1%) Causal Relationship Unknown**

***Central Nervous System***: Paraesthesia, hallucinations, dream abnormalities, vertigo.

***Dermatological***: Toxic epidermal necrolysis, photoallergic skin reactions.

***Special Senses:*** Conjunctivitis, diplopia, optic neuritis, cataracts.

***Haematological***: Bleeding episodes (e.g. epistaxis, menorrhagia).

***Metabolic/endocrine:*** Gynaecomastia, hypoglycaemic reaction, acidosis.

***Renal:*** Nephrotoxicity in various forms, including interstitial nephritis, nephrotic syndrome and renal failure.

***Hepatic***: Abnormal liver function, hepatic failure, hepatitis and jaundice.

***Cardiovascular:*** Arrhythmias (sinus tachycardia, sinus bradycardia).

***Allergic***: Serum sickness, lupus erythematosus syndrome, Henoch-Schönlein vasculitis, angioedema.

**Additional Post-Marketing Adverse Reactions**
Adverse reactions have been reported during post-approval use of Brufen. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to Brufen exposure.

***Gastrointestinal***: Exacerbation of Colitis and Crohn's Disease (see 'CONTRAINDICATIONS'). Pancreatitis has been reported very rarely. A transient sensation of burning in the mouth or throat may occur with ibuprofen syrup.

## DOSAGE AND ADMINISTRATION

After assessing risk/benefit ratio in each individual patient, the lowest effective dose for the shortest duration should be used.

Adult
The recommended initial daily dose of ibuprofen is 1,200-1,600 mg in three to four divided doses, with food or fluids. The dose may be taken on an empty stomach. It is recommended that patients with sensitive stomachs take ibuprofen with food.

For acute exacerbations of rheumatoid arthritis and osteoarthritis in patients already on treatment with ibuprofen, a maximum daily dosage of 2,400 mg may be prescribed, reverting to a maximum of 1,600 mg daily once the patient is stabilised.

Primary dysmenorrhoea
The initial dose is 400-800 mg at the first sign of pain or menstrual bleeding, then 400 mg 4-6 hourly with a maximum total daily dose of 1,600 mg.

Children
The dose is 20-40 mg/kg of bodyweight in divided doses according to the severity of the disease. This can be achieved as follows:

| | |
|---|---|
| 6 months - 1 year | 2.5 mL (50 mg) up to three times a day |
| 1 - 2 years | 2.5 mL (50 mg) three to four times a day |
| 3 - 7 years | 5 mL (100 mg) three to four times a day |
| 8 - 12 years | 10 mL (200 mg) three to four times a day |

Maintenance dose
In all indications the dose should be adjusted for each patient and the smallest dose that results in acceptable control of the symptoms employed. In general, patients with rheumatoid arthritis and osteoarthritis tend to require higher doses than patients with other conditions.

Elderly Population
In elderly patients receiving 600 - 1,200 mg daily ibuprofen appeared to be well tolerated. However, since elderly patients may have a degree of impaired liver or renal function the adult dosage should be used with caution.

Tablet Formulation
Take ibuprofen tablets 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.

Suspension Formulation
Ensure the bottle is thoroughly shaken before use. A transient sensation of burning in the mouth or throat may occur with ibuprofen syrup.

Impaired Liver Function
Ibuprofen should be used with caution in patients with impaired liver function (see 'PRECAUTIONS').

Impaired Renal Function
Ibuprofen should be used with caution in patients with impaired renal function (see 'PRECAUTIONS').

Cardiovascular
Patients on long term treatment should be reviewed regularly with regards to efficacy, risk factors and ongoing need for treatment.

## OVERDOSAGE

Symptoms include nausea, abdominal pain and vomiting, dizziness, convulsion and rarely, loss of consciousness. Clinical features of overdose with ibuprofen which may result are depression of the central nervous system and the respiratory system.

There is no specific antidote to ibuprofen.

For advice on the management of overdose please contact the Poisons Information centre. In Australia please call 13 11 26 and in New Zealand 0800 764 766.

## PRESENTATION AND STORAGE CONDITIONS

Tablets: 400 mg white, pillow-shaped, film-coated tablet; containing the following inactive ingredients: microcrystalline cellulose, croscarmellose sodium, lactose monohydrate, colloidal anhydrous silica, sodium lauryl sulfate, magnesium stearate, hypromellose, purified talc and titanium dioxide.

Available in a bottle* containing 10, 20 or 50 tablets or blister pack containing, 30, 40*, or 60* tablets.

Store below 25°C. Protect from moisture.

Syrup 100 mg/5 mL: orange-coloured, orange-flavoured syrup suspension, containing the following inactive ingredients: sucrose, methyl hydroxybenzoate, propyl hydroxybenzoate, sodium benzoate, citric acid monohydrate, agar, glycerol, sorbitol solution (70%) (non-crystallising), light kaolin, polysorbate 80, sunset yellow FCF CI 15985, orange flavour D71BBA and purified water.

Available in 100 mL and 200 mL glass bottle* or 200 mL plastic bottle*.

Store below 25°C.

*Presentation not currently marketed.

**NAME AND ADDRESS OF THE SPONSOR**

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Millers Point, NSW 2000
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**POISON SCHEDULE OF THE MEDICINE**
S4 - Prescription Only Medicine

**DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (the ARTG)**
BRUFEN Ibuprofen 400 mg tablet blister pack: 12 November 2001
BRUFEN SYRUP Ibuprofen 100 mg/5 mL oral liquid bottle: 15 April 1993

**DATE OF MOST RECENT AMENDMENT:** 31 July 2017

Version 13