Brufen® Tablets 200mg

Ibuprofen 200mg film-coated tablets
Antipyretic, Analgesic & Anti-inflammatory Agent

Indications

Brufen® is indicated for its anti-inflammatory and analgesic effect in the treatment of rheumatoid arthritis, osteoarthritis and allied conditions, non-articular rheumatism and soft tissue injuries. Brufen® is also indicated for its analgesic effect in the relief of mild to moderate pain such as dysmenorrhoea, dental pain, post-operative pain and in the relief of migraine headache. Its antipyretic activity is effective in reducing fever.

Dosage & Administration

Adults and adolescents older than 12 years (≥ 40kg)

The recommended initial dosage is 1200mg – 1800mg daily in divided doses. Some patients can be maintained on 600 – 1200mg daily. Generally, the maximum total daily dose of Brufen® should not exceed 2400mg in divided doses.

Paediatric population

The recommended dose of Brufen® is 20mg/kg of body weight daily in divided doses, but in juvenile rheumatoid arthritis the dosage may be increased to 40mg/kg body weight daily in divided doses, in severe cases. Not recommended for children weighing less than 7kg.

Elderly population

No special dosage modifications are required for elderly patients unless renal or hepatic function is impaired, in which case the dosage should be assessed individually. Caution should be taken with dosage in this group.

Method of administration

In order to achieve a faster onset of action, the dose may be taken on an empty stomach. It is recommended that patients with sensitive stomachs take ibuprofen with food.

Take Brufen® tablets with plenty of fluid. Brufen® tablets should be swallowed whole and not chewed, broken, crushed or sucked on to avoid oral discomfort and throat irritation.

Contraindications

- Known hypersensitivity to the active substance or to any of the inactive ingredients.
- Ibuprofen should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs.
- Severe heart failure (NYHA IV).
- Severe liver failure.
- Severe renal failure (glomerular filtration below 30mL/min).
- Conditions involving a tendency to bleeding.
- History of gastrointestinal bleeding or perforation, related to previous NSAID therapy.
- Active, or a history of, ulcerative colitis, Crohn's disease, recurrent peptic ulceration or gastrointestinal hemorrhage (defined as two or more distinct episodes of proven ulceration or bleeding).
- During the third trimester of pregnancy.

Warnings and Precautions

General Precautions

Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see Dosage and Administration and Gastrointestinal and cardiovascular risks below).

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

On prolonged use of any painkillers, headache may occur that must not be treated with increased doses of the medicinal product.

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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.

Information Related to Excipients
Brufen® Tablets 200mg contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Elderly Population
Elderly patients have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation, which may be fatal.

Gastrointestinal Bleeding, Ulceration and Perforation
NSAIDs should be given with care to patients with a history of peptic ulceration and other gastrointestinal disease since their conditions may be exacerbated (see Contraindications).

Gastrointestinal bleeding, ulceration or perforation has been reported with all NSAIDs at any time during treatment. These adverse events can be fatal and may occur with or without warning symptoms or a previous history of serious gastrointestinal events.

The risk of gastrointestinal bleeding, ulceration or perforation is higher with increasing Brufen® doses in patients with a history of ulcers, particularly if complicated with hemorrhage or perforation, 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, as well as patients requiring concomitant low dose acetylsalicylic acid/aspirin, or for other drugs likely to increase gastrointestinal risk (see **Drug Interactions**).

The concomitant administration of Brufen® and other NSAIDs, including cyclooxygenase-2 (Cox-2) selective inhibitors, should be avoided due to the increased risk of ulceration or bleeding (see Drug Interactions).

Patients with a history of gastrointestinal disease, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding) in the initial stages of treatment.

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 acetylsalicylic acid/aspirin (see Drug Interactions).

If gastrointestinal bleeding or ulceration occurs in patients receiving Brufen®, the treatment should be withdrawn.

Respiratory Disorders
Caution is required if Brufen® is administered to patients suffering from, or with a previous history of, bronchial asthma, chronic rhinitis or allergic diseases since Brufen® has been reported to cause bronchospasm, urticaria or angioedema in such patients.

Cardiac, Renal and Hepatic Impairment
Caution is required in patients with renal, hepatic or cardiac impairment since the use of
NSAIDs may result in deterioration of renal function. The habitual concomitant intake of various painkillers further increases this risk. For patients with renal, hepatic or cardiac impairment, use the lowest effective dose, for the shortest possible duration and monitor renal function especially in long-term treated patients (see Contraindications).

Cardiovascular and Cerebrovascular Effects
Brufen® should be given with care to patients with a history of heart failure or hypertension since edema has been reported in association with Brufen® administration.

Non-selective NSAIDs may be associated with a small increase in the absolute risk of cardiovascular events (e.g. myocardial infarction and stroke), especially when used at high doses for long-term treatment.

Clinical studies suggest that use of Brufen®, particularly at a high dose (2,400 mg/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 Brufen® (e.g. ≤1,200 mg/day) is associated with an increased risk of arterial thrombotic events, particularly myocardial infarction. All NSAIDs should be prescribed at the lowest effective dose and the duration of treatment should be periodically reviewed and kept as short as possible.

Patients with uncontrolled hypertension, congestive heart failure, established ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease should only be treated with Brufen® 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, hyperlipidemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400mg/day) are required.

All NSAIDS should not be used perioperatively in patients who have recently undergone coronary artery bypass graft (CABG) surgery and revascularization procedures.

Dermatological Effects
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. Patients appear to be at highest risk of these reactions early in the course of therapy. In the majority of cases, the onset of the reaction occurs within the first month of treatment. Brufen® should be discontinued at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity.

Exceptionally, 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.

Renal Effects
Caution should be used when initiating treatment with Brufen® in patients with considerable dehydration. There is a risk of renal impairment especially in dehydrated children, adolescents and the elderly.

As with other NSAIDs, long-term administration of Brufen® has resulted in renal papillary necrosis and other renal pathologic changes. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of NSAIDs may cause a dose-dependent 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 NSAIDs therapy is usually followed by recovery to the pretreatment state.

Hematological Effects
Brufen®, like other NSAIDs, can inhibit platelet aggregation and prolong bleeding time of normal being.

Aseptic Meningitis
Aseptic meningitis has been observed on rare occasions in patients on Brufen® 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.

Drug Interactions

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

Anti-hypertensives, 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.

Lithium
NSAIDs may decrease elimination of lithium.

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

Anti-coagulants
NSAIDs may enhance the effects of anticoagulants, such as warfarin.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs) (e.g. clopidogrel and ticlopidine)
Increased risk of gastrointestinal bleeding with NSAIDs.

Aminoglycosides
NSAIDs may decrease the excretion of aminoglycosides.

Acetylsalicylic acid/Aspirin
As with other products containing NSAIDs, concomitant administration of Brufen® and acetylsalicylic acid/aspirin is not generally recommended because of the potential of increased adverse effects.

Experimental data suggest that Brufen® may competitively inhibit the effect of low dose acetylsalicylic acid/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 Brufen® use (see Pharmacodynamic Properties).

Cardiac Glycosides
NSAIDs may exacerbate heart failure, reduce glomerular filtration rate and increase plasma cardiac glycoside levels.

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

Cyclosporine
Increased risk of nephrotoxicity with NSAIDs.

Corticosteroids
Increased risk of gastrointestinal ulceration or bleeding with NSAIDs.

Cox-2 Inhibitors and other NSAIDs
Concomitant use with other NSAIDs, including cyclooxygenase-2 selective inhibitors, should be avoided due to the potential for additive effects (see Warnings and Precautions).

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

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.

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 Brufen®.

Tacrolimus
Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

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 Brufen®.

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

Pregnancy and Lactation

Pregnancy
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo/fetal 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/fetal 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, Brufen® should not be given unless clearly necessary. If Brufen® 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 fetus 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, Brufen® is contraindicated during the third trimester of pregnancy.

Labor and Delivery
Administration of Brufen® is not recommended during labor and delivery.

The onset of labor may be delayed and the duration increased with a greater bleeding tendency in both mother and child.

Breast-feeding
In the limited studies so far available, Brufen® appears in the breast milk in very low concentrations. Brufen® is not recommended for use in nursing mothers.

Female Fertility
The use of Brufen® 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 Brufen® should be considered.

Effects on Ability to Drive and To 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. This applies to a greater extent in combination with alcohol.

Adverse Reactions
The pattern of adverse events reported for Brufen® is similar to that for other NSAIDs.

Gastrointestinal disorders
The most commonly observed adverse events are gastrointestinal in nature. Nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, melena, hematemesis, ulcerative stomatitis, gastrointestinal hemorrhage and exacerbation of colitis and Crohn's disease (see Contraindications) have been reported following Brufen® administration. Less frequently, gastritis, duodenal ulcer and gastric ulcer, and gastrointestinal perforation have been observed.

Immune system disorders
Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnea, 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).

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.

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").

Cardiac and vascular disorders
Clinical studies suggest that use of ibuprofen (particularly at a high dose of 2400mg/day may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke, see Warnings & Precautions).
The following adverse reactions possibly related to ibuprofen ad displayed by MedDRA frequency convention and system organ classification. Frequency groupings are classified according to the subsequent conventions: very common (≥ 1/10), Common (≥ 1/100 to <1/10), Uncommon (≥ 1/1,000 to <1/100), Rare (≥ 1/10,000 to <1/1,000), Very rare (<1/10,000) and Not known (cannot be estimated from the available data).

System organ class	Frequency	Adverse reaction
Infections and infestations	Uncommon	Rhinitis
	Rare	Meningitis aseptic (see Warnings and Precautions)
Blood and lymphatic system disorders	Rare	Leukopenia, thrombocytopenia, neutropenia, agranulocytosis, aplastic anemia and hemolytic anemia
Immune system disorders	Uncommon	Hypersensitivity
	Rare	Anaphylactic reaction
Psychiatric disorders	Uncommon	Insomnia, anxiety
	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, diarrhea, nausea, vomiting, abdominal pain, flatulence, constipation, melena, hematemesis, gastrointestinal hemorrhage
	Uncommon	Gastritis, duodenal ulcer, gastric ulcer, mouth ulceration, gastrointestinal perforation
	Very rare	Pancreatitis
	Not known	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)
	Not Known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)
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 Warnings and Precautions)
Vascular disorders	Very rare	Hypertension

Overdosage

Toxicity

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

Symptoms

Most patients who have ingested significant amounts of Brufen® 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, apnea and depression of the CNS and respiratory system have also been rarely reported. Cardiovascular toxicity, including hypotension, bradycardia and tachycardia, has 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. In serious poisoning metabolic acidosis may occur.

Treatment

There is no specific antidote for Brufen® overdose. Gastric emptying followed by supportive measures is recommended if the quantity ingested exceeds 400 mg/kg within the previous hour.

Pharmacologic Properties

Pharmacodynamic Properties

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

Experimental data suggest that Brufen® may competitively inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. Some pharmacodynamics studies show that when single doses of Brufen® were taken within 8 h before or within 30 min after immediate release aspirin dosing (81 mg), a decreased effect of acetylsalicylic acid/aspirin 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/aspirin cannot be excluded. No clinically relevant effect is considered to be likely for occasional Brufen® use (see Drug Interactions).

Pharmacokinetic Properties

Brufen® is rapidly absorbed from the gastrointestinal tract, peak serum concentrations occurring one to two hours after administration. The elimination half-life is approximately two hours.

Brufen® is metabolized in the liver to two inactive metabolites and the kidney excretes these, together with unchanged ibuprofen, either as such or as conjugates. Excretion by the kidney is both rapid and complete.

Brufen® is extensively bound to plasma proteins.

Storage

The shelf life of the product is 3 years.
Do not store above 25 °C.

Pack size

Brufen® Tablets 200mg — 25/30/50/100/500 tablets
Not all presentation may be marketed.

Manufactured By

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Abbott

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