

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

IBUPROFEN, coated tablets 200 mg, Teva

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each coated tablet contains 200 mg of ibuprofen.

Excipient with known effect: Lactose

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

White, capsule shaped coated tablets with no markings.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

IBUPROFEN is indicated for analgesic and anti-inflammatory effect 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, IBUPROFEN is indicated in periarticular conditions such as frozen shoulder (capsulitis), bursitis, tendonitis, tenosynovitis and low-back pain.

IBUPROFEN can also be used in soft-tissue injuries such as sprains and strains.

IBUPROFEN is also indicated for its analgesic effect in the relief of mild to moderate pain such as dysmenorrhoea, dental and post-operative pain.

4.2 Dose and method of administration

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

Adults:

The recommended initial daily dose of IBUPROFEN is 1200-1800mg per day in divided doses. Some patients can be maintained on 600 -1200mg per day. In severe or acute conditions it can be advantageous to increase the dosage until the acute phase is brought under control, providing that the total daily dose does not exceed 2400mg in divided doses.

Special Populations:

Children:

The daily dosage of IBUPROFEN is 20mg per kg of body weight in divided doses. In juvenile rheumatoid arthritis up to 40mg per kg of bodyweight in divided doses may be given. In children weighing less than 30kg the total dose should not exceed 500mg in a 24 hour period.

Elderly:

Elderly patients are more prone to adverse effects. Caution must be taken with dosage in this group.

Renal impairment:

Caution must be taken in with dosage for patients in this group. (See **4.3 Contraindications** and **4.4 Special warning and precautions for use.**)

Hepatic impairment:

Caution must be taken in with dosage for patients in this group. (See **4.3 Contraindications** and **4.4 Special warning and precautions for use.**)

4.3 Contraindications

Known hypersensitivity to ibuprofen.

Hypersensitivity (e.g. asthma, rhinitis or urticaria) to aspirin or other non-steroidal anti-inflammatory drugs. As with other non-steroidal anti-inflammatory agents, ibuprofen should not be given to patients vulnerable to gastrointestinal ulceration and bleeding and haemorrhagic diathesis.

History of gastrointestinal bleeding or perforation, related to previous NSAID therapy.

During the third trimester of pregnancy. (see **4.6 Fertility, pregnancy and lactation**)

Severe heart failure.

Severe liver failure.

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

Conditions involving an increased tendency or active bleeding.

(See **4.4 Special warnings and precautions for use** for more information on above contraindications.)

4.4 Special warnings and precautions for use

Ibuprofen should not be given to patients in whom aspirin and other non-steroidal anti-inflammatory medicines induce the symptoms of asthma, rhinitis or urticaria. Adverse ophthalmological effects have been observed with non-steroidal anti-inflammatory agents. Any patient who develops visual disturbances during treatment with ibuprofen should have an ophthalmological examination. In patients with systemic lupus erythematosus the risk/benefit ratio has to be analysed before prescribing ibuprofen. This is a danger due to the possibility of severe generalised hypersensitivity reaction.

Non-steroidal anti-inflammatory agents have been reported to cause nephrotoxicity in various forms; interstitial nephritis, nephrotic syndrome and renal failure. In patients with renal cardiac or hepatic impairment, caution is required since the use of non-steroidal anti-inflammatory agents may result in deterioration of renal function. The dose should be kept as low as possible and renal function should be monitored in these patients.

Cardiovascular Thrombotic Events

Epidemiological data suggest that use of ibuprofen, particularly at a high dose (2400 mg/ daily) and in long term treatment, may be associated with a small increased risk of arterial thrombotic events such as myocardial infarction or stroke. Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200 mg daily) is associated with an increased risk of arterial thrombotic events, particularly myocardial infarction.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration. Similar consideration should be made before initiating longer-term treatment of

patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

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 the onset of new hypertension or worsening of pre-existing hypertension and patients taking anti-hypertensives 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

All NSAIDs can cause gastrointestinal discomfort and rarely serious, potentially fatal gastrointestinal effects such as ulcers, bleeding and perforation, which may increase with dose or duration of use but can, occur at any time without warning. Upper GI ulcers, gross bleeding or perforation caused by NSAIDs occur approximately 1% of patients treated for 3-6 months and in about 2-4% 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.

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 the signs and symptoms of serious gastrointestinal toxicity.

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

Severe Skin Reactions

NSAIDs may 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 sign of hypersensitivity.

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.

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.

Pregnancy:

During the first and second trimester of pregnancy, ibuprofen should not be given unless clearly necessary. If ibuprofen is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low as possible and the duration of treatment as short as possible.

Non-steroidal anti-inflammatory drugs inhibit prostaglandin synthesis and, when given in the latter part of pregnancy, may cause closure of the foetal ductus arteriosus, foetal renal impairment, inhibition of platelet aggregation and delay labour and birth. Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or embryo/fetal development. Continuous treatment with non-steroidal anti-inflammatory drugs during the last trimester of pregnancy should be given on sound indications. During the last few days before expected birth, agents with an inhibitory effect on prostaglandins synthesis should be avoided. (see **4.6 Fertility, pregnancy and lactation**)

4.5 Interaction with other medicines and other forms of interaction

ACE inhibitors

Ibuprofen, like other NSAIDs can reduce the antihypertensive effect 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 **4.4 Special warnings and precautions for use**)

Lithium

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.

Anti-platelet agents

Increased risk of gastrointestinal bleeding

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

function with anticoagulant effect of warfarin. Ibuprofen should only be used in patients taking warfarin if absolutely necessary. Patients taking this combination must be closely monitored.

Aminoglycosides

NSAIDs may decrease the excretion of aminoglycosides.

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.

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 inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use (see **5. Pharmacological Properties**).

Cyclosporin 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 hypoglycaemia in patients on sulfonylurea medications receiving ibuprofen.

Zidovudine

Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and hematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Methotrexate

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.

4.6 Fertility, pregnancy and lactation

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.

Pregnancy

Category C

Non-steroidal anti-inflammatory drugs inhibit prostaglandin synthesis and, when given in the latter part of pregnancy, may cause closure of the foetal ductus arteriosus, foetal renal impairment, inhibition of platelet aggregation and delay labour and birth. Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or embryo/fetal development. Continuous treatment with non-steroidal anti-inflammatory drugs during the last trimester of pregnancy should be given on sound indications. During the last few days before expected birth, agents with an inhibitory effect on prostaglandins synthesis should be avoided.

Some data from epidemiological studies suggest an increased risk of miscarriage after use of a prostaglandin synthesis inhibitor (such as NSAIDs) in early pregnancy. In animals, administration of prostaglandin synthesis inhibitors has been shown to result in increased pre- and post-implantation loss. . During the first and second trimester of pregnancy, ibuprofen should not be given unless clearly necessary. If ibuprofen is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low as possible and the duration of treatment as short as possible.

Lactation

In the limited studies so far available, ibuprofen appears in breast milk in very low concentrations and is unlikely to affect the breast fed infant adversely. However, it is not recommended for nursing mothers unless the expected benefits to the mother outweigh the potential risk to the neonate.

4.7 Effects on ability to drive and use machines

Following treatment with ibuprofen, the reaction time of patients may be affected. NSAIDs may cause dizziness, drowsiness, fatigue and visual disturbances. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

The most common (greater than 1%) adverse effects reported include: nausea, epigastric pain, heartburn, diarrhoea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of the GI tract (bloating and flatulence), tinnitus, oedema, fluid retention, dizziness, headache, nervousness, rash, pruritus and decreased appetite.

Other less common (less than 1%) reactions include: depression, insomnia, confusion, somnolence, aseptic meningitis with fever and coma, vesiculobullous eruptions, urticaria, alopecia, gastrointestinal haemorrhage, pancreatitis, gastritis, jaundice, abnormal liver function tests, amblyopia, fever, chills, anaphylaxis, bronchospasm, melaena, neutropenia, agranulocytosis, aplastic anaemia and decrease in haemoglobin and haematocrit.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

Vomiting/emesis is no longer recommended for the treatment of overdose. Therefore the treatment advice should be:

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

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Anti-inflammatory and anti-rheumatic products, non-steroids, Propionic acid derivatives, ATC Code: M01AE

Mechanism of action:

Ibuprofen is a non-steroidal anti-inflammatory agent. Its mode of action, like that of other non-steroidal 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 human and animal studies. These properties provide symptomatic relief of inflammation and pain.

5.2 Pharmacokinetic properties

Ibuprofen is well absorbed after oral administration. A single dose of 200mg taken on an empty stomach by volunteers produced peak serum levels after approximately 45 minutes. When taken after food, the absorption of ibuprofen was slower, and peak serum levels appeared between 1.5 and 3 hours.

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

Approximately 99% of ibuprofen is protein bound. The high protein binding should be kept in mind when prescribing ibuprofen together with other protein bound drugs that bind to the same site on human serum albumin.

Approximately 90% of ibuprofen is metabolised to two major metabolites (A and B). These are: Metabolite A (+) 2-4-(2-hydroxy-2-methylpropylphenyl) propionic acid and Metabolite B (+) 2-4-(2-carboxypropylphenyl) propionic acid. Both metabolites are dextrorotary and do not exhibit anti-inflammatory and analgesic activity.

Patients with rheumatoid arthritis and normal volunteers were given 800mg of ibuprofen as a single dose. After 14 to 24 hours the plasma levels of ibuprofen and metabolites was less than 0.25mcg/mL.

The major route of excretion is via the kidney, with 95% of ibuprofen being excreted in the urine within 24 hours of a single dose of 500mg. Of this 35 % was excreted as metabolite A (15% free, 20%

conjugated), 51% as metabolite B (42% free, 9% conjugated) and 9% as ibuprofen (1% free, 8% conjugated).

The plasma half-life of ibuprofen is between 1.9 to 2.2 hours.

5.3 Preclinical safety data

No information available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide, hypromellose, lactose, magnesium stearate, potato starch, sodium starch glycolate, carnuba wax, maize starch, purified talc, sucrose, titanium di-oxide

IBUPROFEN tablets are gluten free.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Blister pack of 1000 tablets (Prescription Medicine)

Blister packs of 30, 50 and 100 tablets (Pharmacy Medicine)

Blister pack of 20 tablets (General Sale Medicine)

Not all pack sizes may be marketed

6.6 Special precautions for disposal

No special requirements for disposal.

7. MEDICINE SCHEDULE

Prescription Medicine: 1000 tablet dispensing only pack

Pharmacy Medicine: 30, 50 and 100 tablet packs

General Sale Medicine: 20 tablet pack

8. SPONSOR

Teva Pharma (New Zealand) Limited

PO Box 128244

Remuera

Auckland 1541

Telephone: 0800 800 097

9. DATE OF FIRST APPROVAL

General Sale Medicine: 20 tablet pack: 24th May 2012

Pharmacy Medicine: 30, 50 and 100 tablet packs: 17th November 2011

Prescription Medicine: 1000 tablet dispensing only pack: 23rd June 2011

10. DATE OF REVISION OF THE TEXT

14th Aug 2017

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
Complete data sheet	Reformatted as per SPC style format.
4.4, 4.6	Safety information related to pregnancy, based on recommendation by MARC added as advised by Medsafe.