



## New Zealand Data Sheet

### APO-IBUPROFEN

#### Ibuprofen 200mg Tablets

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#### **Presentation**

Apo-Ibuprofen is a round biconvex tablet with a yellow film coating. The tablet is identified "IBU" over "200" on one side and is 9.68mm in diameter.

#### **Uses**

#### **Actions**

Apo-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.

#### **Pharmacokinetics**

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.

#### **Indications**

Apo-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, Apo-Ibuprofen is indicated in periarticular conditions such as frozen shoulder (capsulitis), bursitis, tendonitis, tenosynovitis and low-back pain. Apo-Ibuprofen can also be used in soft-tissue injuries such as sprains and strains.

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

### Dosage and 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 Apo-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.

**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 and also in patients with renal impairment or impaired liver function.

### 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.

### Warnings and Precautions

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

Observational studies have indicated that non-selective NSAIDs may be associated with an increased risk of serious cardiovascular events, including myocardial infarction and stroke which may increase with dose or duration of use. Patients with cardiovascular disease or cardiovascular risk factors may also be at greater risk. To minimise 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).

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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.

### **Use in Pregnancy and Lactation**

#### 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. 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.

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.

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### Effects on ability to drive and operate machinery

Ibuprofen is presumed to be safe, or unlikely to inhibit the ability to drive or operate machinery.

### Adverse 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.

### Interactions

Ibuprofen, like other NSAIDs can reduce the antihypertensive effect ACE inhibitors and beta blockers with possible loss of blood pressure control and can attenuate the natriuretic effects of thiazide diuretics and frusemide.

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.

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

NSAIDs may increase plasma cardiac glycoside levels. Care should therefore be taken in patients treated with cardiac glycosides.

### Overdosage

Clinical features of overdose with ibuprofen that may result are depression of the central nervous system and the respiratory system.

In cases of acute overdose, the stomach should be emptied by vomiting or lavage, although little of the drug will be likely to be recovered if it is more than an hour since ingestion. Because the drug is acidic and excreted in the urine, it is theoretically beneficial to administer alkali and induce diuresis. In addition to supportive measures, the use of oral activated charcoal may help reduce the absorption of ibuprofen.

### Pharmaceutical Precautions

Shelf life 36 months from date of manufacture

Store below 25°C.

Protect from heat, light and moisture.



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### Medicine Classification

Pharmacy only medicine for packs of 30, 90 and 100 tablets.  
Prescription only medicine for packs of 500 tablets.

### Package Quantities

Bottle packs of 100 and 500 tablets.  
Blister packs of 30 and 90 tablets.

### Further Information

Nil

### Name and Address

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### Date of Preparation

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