

ULTRAFEN

Caplets & Liquid capsules

Composition

Each caplet contains Ibuprofen 200, 400 or 600 mg.

Each liquid capsule (LC) contains:

Ibuprofen 400 mg.

Action

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 400 mg tablet is equivalent to that from two 200 mg tablets.

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 unknown if ibuprofen enters the CSF or is excreted in milk.

Protein binding

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

Metabolism

About 90% of ibuprofen is metabolised to two major metabolites (A and B); 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 ibuprofen 800 mg as a single dose. After 14 to 24 hours, the plasma levels of ibuprofen and metabolites were less than 0.25 microgram/mL.

Excretion

The kidney is the major route of excretion. 95% of ibuprofen 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

- Ultrafen is indicated for the treatment of rheumatoid arthritis and osteoarthritis.
- It is indicated both in the treatment of acute flares and in the long-term management of these diseases.

- Ultrafen is indicated for the relief of mild to moderate pain, and for the treatment of primary dysmenorrhea.

Contraindications

Ibuprofen should not be used in patients who have previously exhibited hypersensitivity, or in individuals with the syndrome of nasal polyps, angioedema, bronchospastic reactivity to acetylsalicylic acid or other NSAID's (anaphylactoid reactions have occurred in such patients).

Warnings

Ibuprofen should be administered under close supervision to patients with a history of upper gastrointestinal tract disease.

Pregnancy

Category B (1st and 2nd trimesters)

Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

Category D (If used in 3rd trimester)

There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Nursing Mothers

Safety of use in breastfeeding has not been established. Ibuprofen is not recommended for use in nursing mothers.

Adverse Reactions

Gastrointestinal: Epigastric pain, heartburn, diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of gastrointestinal tract, GI bleeding and activation of peptic ulcer.

Central Nervous System: Dizziness, headache, nervousness, convulsions pain in the spinal column, depression and drowsiness and aseptic meningitis.

Dermatological: Rash (including maculopapular type), pruritus.

Special Senses: Tinnitus.

Metabolic/Endocrine: Decreased appetite.

Cardiovascular: Edema, fluid retention (generally responds promptly to drug discontinuation).

Hematological: Neutropenia, agranulocytosis, aplastic anemia, hemolytic anemia, thrombocytopenia, decreased hemoglobin and hematocrit.

Allergic: Fever

Liver: Abnormalities in liver function tests and hepatotoxicity.

Lung: Provoke bronchospasm in patients with asthma.

Blood: Hematuria, cystitis

Kidney: Acute renal failure, intestinal nephritis, and nephritic syndrome.

Eyes:

Blurred vision, changes in visual colour perception and toxic amblyopic

Other: Stiffness.

Precautions

Blurred and/or diminished vision, scotomata, and changes in color vision have been reported. If a patient develops such complaints while receiving ibuprofen, the drug should be discontinued and the patient should have an ophthalmological examination that includes central visual fields and color vision testing.

Patients should be cautioned about engaging in activities requiring mental alertness and motor coordination, such as driving a car.

Patients taking Ibuprofen should report to their physician's signs or symptoms of gastrointestinal ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain, or edema.

Fluid retention and edema have been reported in association with ibuprofen. Therefore, the drug should be used with caution in patients with a history of cardiac decompensation or hypertension.

Since primarily the kidneys, patients with, eliminate ibuprofen significantly, impaired renal function should be closely monitored, and a reduction in dosage should be anticipated to avoid drug accumulation.

Ibuprofen should be used with caution in persons with intrinsic coagulation defects and those on anticoagulant therapy.

In order to avoid exacerbation of disease or adrenal insufficiency, patients who have been on prolonged corticosteroid therapy should have their therapy reduced slowly, rather than discontinued abruptly, when Ibuprofen is added to the treatment regimen.

As with other NSAID's, borderline elevations of one or more liver tests may occur in up to 15% of patients. These abnormalities may progress, remain essentially unchanged, or be transient with continued therapy.

Patients with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has been reported, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with Ibuprofen. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with ibuprofen, as with other NSAID's. Although such reactions are rare, if abnormal liver tests persist or worsen, or clinical signs and symptoms consistent with liver disease develop, or systemic manifestations occur (e.g. eosinophilia, rash, etc.), Ibuprofen should be discontinued. In cross-study comparisons with doses ranging from 1,200-3,200 mg daily for several weeks, a slight dose- response decrease in hemoglobin/hematocrit was noted. Aseptic meningitis with fever and coma has been observed 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. If signs or symptoms of meningitis develop in a patient on Ibuprofen therapy, the possibility of its being related to Ibuprofen should be considered.

Drug Interactions

Ibuprofen/Coumarin-type Anticoagulants

Because bleeding has been reported when ibuprofen and other NSAID's have been administered to patients on coumarin-type anticoagulants, physicians should exercise caution when administering Ibuprofen to patients on anticoagulants.

Ibuprofen / Acetylsalicylic Acid

Animal studies have demonstrated that acetylsalicylic acid administered with NSAID's causes a decrease in blood levels and activity of non-salicylate drugs. Since concomitant use offers no therapeutic advantage, such combinations should be avoided.

Ibuprofen / Methotrexate

Animal studies indicate that ibuprofen, as well as other NSAID's, may enhance the toxicity of methotrexate. Caution should be used if Ibuprofen is administered concomitantly with methotrexate.

Ibuprofen / furosemide

Clinical studies, as well as random observations, have shown that ibuprofen can reduce the natriuretic effect of furosemide and thiazides in some patients. During concomitant therapy with Ibuprofen, patients should be observed closely for signs of renal failure, as well as to assure diuretic efficacy.

Ibuprofen / Lithium

Ibuprofen produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. Therefore, when Ibuprofen and lithium are administered concurrently, patients should be observed carefully for signs of lithium toxicity.

Dosage and Administration

The total daily dosage of Ultrafen should not exceed 3,200 mg. If gastrointestinal complaints occur, Ultrafen should be administered with meals or milk.

Rheumatoid Arthritis and Osteoarthritis (300 mg q.i.d or 400 mg, 600 mg or 800 mg t.i.d or q.i.d)

The dose should be tailored to each patient, and may be lowered or raised depending on the severity of symptoms at time of initiating drug therapy or as the patient responds or fails to respond.

In general, patients with rheumatoid arthritis seem to require higher doses of Ultrafen than do patients with osteoarthritis. The smallest dose of Ultrafen that yields acceptable control should be employed. A linear blood level dose-response relationship exists with single doses up to 800 mg.

In chronic conditions, a therapeutic response to therapy with Ultrafen is sometimes seen within a few days to a week, but most often is observed by two weeks. After a satisfactory response has been achieved, the patient's dose should be reviewed and adjusted as required.

Mild to Moderate Pain 400 mg, every 4-6 hours, as necessary for the relief of pain.

Primary Dysmenorrhea 400 mg, every 4 hours as necessary, beginning with the earliest onset of pain.

Over Dosage

The most likely symptoms of over dosage are epigastric pain and nausea. If recently taken, gastric lavage will remove any unabsorbed Ibuprofen. Electrolytes may be corrected by intravenous infusions, if necessary. There is no specific antidote to Ibuprofen.

Presentation

Ultrafen 200

Box of 20 caplets.

Ultrafen 400

Box of 20 caplets.

Ultrafen 600

Box of 10 caplets.

Ultrafen LC

Box of 10 liquid capsules.