

Fenpaed

Ibuprofen 100 mg/5 mL Oral Suspension

Presentation

FENPAED Oral Suspension is a white, strawberry flavoured suspension containing 100 mg ibuprofen per 5 mL

Uses

Actions

Ibuprofen is a nonsteroidal anti-inflammatory agent (NSAID) 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, and 20 mL of a 2% FENPAED Oral Suspension.

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 ibuprofen enters the CSF. According to reports only minimal amounts are excreted in breast milk.

Protein binding:

99% of ibuprofen is protein bound. The high protein binding of ibuprofen should be borne in mind when rescribing 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 ((+)-2-(2-hydroxy-2-methylpropylphenyl) propionic acid) and B ((+)-2-(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 µg/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

FENPAED Oral Suspension is indicated for its 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. FENPAED Oral Suspension can also be used in soft-tissue injuries such as sprains and strains.

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

In children, FENPAED Oral Suspension is useful for the symptomatic relief of pain and fever in a wide range of indications. It is also indicated for upper respiratory tract and other infections including influenza, bronchitis, tonsillitis, pharyngitis, sinusitis, etc., in conjunction with other appropriate therapies.

Dosage and Administration

The dose should be individualised after assessing the risk/benefit ratio such that the lowest effective dose for the shortest possible duration is used.

Infants and Children

For infants and children a daily oral dose of 20 mg/kg body weight in divided doses. Up to 40 mg/kg body weight daily in divided doses may be recommended in cases of juvenile rheumatoid arthritis (Still's Disease).

In children weighing less than 30 kg, the total daily dose of FENPAED Oral Suspension should not exceed 500 mg.

Examples of typical daily doses are:

Six months - one year:

Dose to be assessed by the physician.

1 - 5 years:

Up to 5 mL given 3 to 4 times a day (total maximum daily dose 20 mL)

5 - 12 years:

Up to 10 mL given 3 to 4 times a day (total maximum daily dose 40 mL)

Adults

Although Ibuprofen tablets are generally used for adults, when there are swallowing difficulties, FENPAED Oral Suspension can be used at an appropriate dosage:

The initial recommended dosage is 1200 - 1800 mg (60 – 90 mL) daily in divided doses. Some patients can be maintained on 600 - 1200 mg (30 mL – 60 mL) daily. 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 dosage does not exceed 2400 mg (120 mL) in divided doses.

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 nonsteroidal anti-inflammatory drugs.
- As with other nonsteroidal anti-inflammatory agents, ibuprofen should not be used in active gastrointestinal bleeding or in the presence of peptic ulceration.
- Pregnancy
- Lactation

Warnings and Precautions

Gastrointestinal Events

All NSAIDs can cause gastrointestinal discomfort and rarely, serious potentially fatal gastrointestinal effects e.g. ulcers, bleeding and perforations, which may increase with dose or duration of use but may occur at any time 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% 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 GI events who may be at greater risk of developing serious GI events e.g. the elderly, those with a history of serious GI events, smoking and alcoholism. When GI bleeding or ulcerations occur in patients receiving NSAIDs the medicine should be withdrawn immediately. Doctors should warn patients about the signs and symptoms of serious GI toxicity.

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

Asthma

Caution is required if ibuprofen is administered to patients suffering from, or with a previous history of, bronchial asthma because ibuprofen has been reported to cause bronchospasm in such patients.

Ophthalmological Monitoring

Adverse ophthalmological effects have been observed with nonsteroidal anti-inflammatory agents; accordingly, patients who develop visual disturbances during treatment with ibuprofen should have an ophthalmological examination.

Impaired Liver Function or a History of Liver Disease

Patients with impaired liver function or a history of liver disease that 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 nonsteroidal anti-inflammatory drugs. 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

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. As with other nonsteroidal anti-inflammatory drugs (NSAIDs) long-term administration of ibuprofen 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 a NSAID may cause a dose-dependent reduction in prostaglandin formation and secondarily in renal blood flow, which may precipitate overt renal decompensation. Therefore in patients with renal, cardiac or hepatic impairment, those taking diuretics and the elderly, caution is required since the use of

NSAIDs 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 Effects

Observational studies have indicated that NSAIDs such as ibuprofen 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 ibuprofen, especially in those with cardiovascular risk factors, the lowest effective dose should be used for the shortest possible duration.

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

Fluid retention and oedema have been reported in association with ibuprofen, therefore, the drug should be used with caution in patients with a history of failure or hypertension.

Hypertension

NSAIDs may lead to the onset of 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.

Severe Skin Reactions

NSAIDs may very rarely cause serious cutaneous adverse events e.g. exfoliative dermatitis, toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) which can be fatal and occur without warning. These serious 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 hypersensitivity.

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.

Withdrawal of Concomitant Steroid Therapy

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 during Pregnancy and Lactation

Category C.

While no teratogenic effects have been demonstrated in animal studies, the use of ibuprofen during pregnancy should be avoided if possible. Congenital abnormalities have been reported in association with ibuprofen administration in man; however these are low in frequency and do not appear to follow any discernible pattern.

Nonsteroidal anti-inflammatory drugs inhibit prostaglandin synthesis and, when given during 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 nonsteroidal anti-inflammatory drugs during the last trimester of pregnancy should only be given on sound indications. During the last few days before expected birth, agents with an inhibitory effect on prostaglandin synthesis should be avoided.

Ibuprofen is not recommended for nursing mothers unless the expected benefits to the mother outweigh the potential risk to the neonate.

Effects on ability to drive and use machines

No adverse effects known.

Adverse Effects

Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of non-specific allergic reaction and anaphylaxis, respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or associated skin disorders including rashes of various types, pruritus, urticaria, purpura, angioedema and less commonly, bullous dermatoses including epidermal necrolysis and erythema multiforme.

More common reactions: (greater than 1%)

Gastrointestinal:

The most frequent type of adverse reactions are gastrointestinal. Gastrointestinal complaints 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), melaena, gastritis and gastrointestinal haemorrhage.

Auditory and vestibular:

Tinnitus, vertigo.

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.

Less common reactions: (less than 1%)

Central nervous system:

Depression, insomnia, 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, pancreatitis, hepatitis, jaundice, abnormal liver function tests.

Haematological:

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

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).

Allergic:

Syndrome of abdominal pain, fever, chills, nausea and vomiting, anaphylaxis, bronchospasm

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

Central Nervous System:

Paraesthesias, hallucinations, dream abnormalities

Dermatological:

Toxic epidermal necrolysis, photoallergic skin reactions, exfoliative dermatitis, Stevens-Johnson syndrome

Special Senses:

Conjunctivitis, diplopia, optic neuritis, cataracts

Haematological:

Bleeding episodes (eg epistaxis, menorrhagia)

Metabolic/endocrine:

Gynaecomastia, hypoglycaemic reaction, acidosis

Renal:

Renal nephrotoxicity in various forms including interstitial nephritis, nephrotic syndrome and renal failure

Hepatic:

Abnormal liver function, hepatitis and jaundice

Cardiovascular:

Arrhythmias (sinus tachycardia, sinus bradycardia)

Allergic:

Serum sickness, lupus erythematosus syndrome, Henoch-Schönlein vasculitis, angioedema

Interactions

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.

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

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 and β -blockers with possible loss of blood pressure control and can attenuate the natriuretic effects of thiazide diuretics and frusemide.

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.

Other analgesics: Avoid concomitant use of 2 or more NSAIDs including aspirin because of the potential of increased adverse effects.

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

Overdosage

Symptoms

Symptoms include nausea, abdominal pain and vomiting, dizziness 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.

Treatment

In cases of acute overdose, the stomach should be emptied by vomiting or lavage, though little drug will likely be recovered if more than an hour has elapsed since ingestion. Because the drug is acidic and is 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

Store below 25 °C. Shake bottle well before use.

Medicines Classification

Prescription Medicine: 200 mL, 500 mL and 1 Litre

Pharmacy Only Medicine: 100 mL, 150 mL, 200 mL and sachet pack

Package Quantities

Amber glass bottle: 100 mL, 150 mL and 200 mL

HDPE bottle: 500 mL and 1 Litre

Sachets: 5 mL per sachet. Packs of 10 and 20 sachets

Further Information

FENPAED Oral Suspension contains the following inactive ingredients: glycerol (E422), Xanthan Gum, Maltitol (E965), Polysorbate 80, Saccharin Sodium (E954), Citric Acid Monohydrate, Sodium Methyl Hydroxybenzoate, Sodium Propyl Hydroxybenzoate, purified water and strawberry flavour.

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