INFORIN

INSTRUCTIONS FOR THE MEDICINAL PRODUCT

Trade name: Inforin.
International Nonproprietary Name: Ibuprofen.
Dosage form: Film coated tablet.
Composition: Each film coated tablet contains:
Active substance:
Ibuprofen 400 mg;
Excipients: lactose monohydrate, maize starch, povidone, cellulose microcrystalline, dimeticone, crosscarmellose sodium, silica colloidal anhydrous, talc, hypromellose,
macrogol 6000, titanium dioxide, color Azorubine 85E 122, color Coch. Rot 80E 124.
Pharmacotherapeutic group: NSAID.
ATCClassification**:** M01AE01.
Pharmacologic property:
Pharmacodynamics:
Ibuprofen is a propionic acid derivative with analgesic, anti-inflammatory and anti-pyretic activity. The drug's therapeutic effect as an NSAID is thought to result from its inhibitory effect on the enzyme cyclo-oxygenase, which results in a marked reduction in prostaglandin synthesis.
Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 hours before or within 30 minutes after immediate release aspirin dosing (81mg), a decreased effect of aspirin on the formation of thromboxane or platelet aggregation occurred. 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.
Pharmacokinetics:
Ibuprofen is rapidly absorbed from the gastrointestinal tract, peak serum concentrations occurring 1-2 hours after administration. The elimination half-life is approximately 2 hours.
Ibuprofen is metabolised in the liver to two inactive metabolites and these, together with unchanged ibuprofen, are excreted by the kidney either as such or as conjugates. Excretion by the kidney is both rapid and complete. Ibuprofen is extensively bound to plasma proteins.
Indications for use:
- Inforin is indicated for its analgesic and anti-inflammatory effects 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, Inforin is indicated in periarticular conditions such as frozen shoulder (capsulitis), bursitis, tendonitis, tenosynovitis and low back pain; Inforin can also be used in soft tissue injuries such as sprains and strains.
- Inforin is also indicated for its analgesic effect in the relief of mild to moderate pain such as dysmenorrhoea, dental and post-operative pain and for symptomatic relief of headache, including migraine headache.

Contraindications:
- Patients with hypersensitivity to the active substance or to any of the excipients;
- Patients who have previously shown hypersensitivity reactions (e.g. asthma, urticaria, angioedema or rhinitis) after taking Inforin, aspirin or other NSAIDs;
- Patients with a history of gastrointestinal bleeding or perforation, related to previous NSAID therapy;
- Patients with active, or history of, recurrent peptic ulcer or gastrointestinal haemorrhage (two or more distinct episodes of proven ulceration or bleeding);
- Patients with conditions involving an increased tendency to bleeding;
- Patients with severe heart failure, hepatic failure and renal failure;
- Inforin is contraindicated during the last trimester of pregnancy.

Precautions: As with other NSAIDs, ibuprofen may mask the signs of infection.
The use of Ibuprofen with concomitant NSAIDs, including cyclooxygenase-2 selective inhibitors, should be avoided due to the increased risk of ulceration or bleeding.
Pregnancy and Nursing Mother:
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo/foetal development.
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 or second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.
Ibuprofen is contraindicated during the third trimester of pregnancy.
In the limited studies so far available, NSAIDs can appear in the breast milk in very low concentrations. NSAIDs should, if possible, be avoided when breastfeeding.

Dosage and directions for use:

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms.

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

Children: The daily dosage of Ibuprofen is 20 mg/kg of body weight in divided doses.

In Juvenile Rheumatoid Arthritis, up to 40 mg/kg of body weight daily in divided doses may be taken.

Not recommended for children weighing less than 7 kg.

Elderly: The elderly are at increased risk of serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy. If renal or hepatic function is impaired, dosage should be assessed individually.

For oral administration. To be taken preferably with or after food.
Side-effects:
Gastrointestinal disorders: The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease have been reported following ibuprofen administration. Less frequently, gastritis has been observed. Gastrointestinal perforation has been rarely reported with ibuprofen use. Pancreatitis has also been reported very rarely.
Immune system disorders: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses (including Stevens- Johnson syndrome, toxic epidermal necrolysis and erythema multiforme).
Cardiac disorders and vascular disorders: Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment. Epidemiological data suggest that use of ibuprofen, particularly at 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.
Other adverse events reported less commonly and for which causality has not necessarily been established includes:
Blood and lymphatic system disorders: Leukopenia, thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia.
Psychiatric disorders: Insomnia, anxiety, depression, confusional state, hallucination.
Nervous system disorders: Optic neuritis, headache, paraesthesia, dizziness, somnolence.
Infections and infestations: Rhinitis and aseptic meningitis (especially in patients with existing autoimmune disorders, such as systemic lupus erythematosus and mixed connective tissue disease) with symptoms of stiff neck, headache, nausea, vomiting, fever or disorientation.
Eye disorders: Visual impairment and toxic optic neuropathy.
Ear and labyrinth disorders: Hearing impaired, tinnitus and vertigo.
Hepatobiliary disorders: Abnormal liver function, hepatic failure, hepatitis and jaundice.
Skin and subcutaneous tissue disorders: Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare), and photosensitivity reaction.
Renal and urinary disorders: Impaired renal function and toxic nephropathy in various forms, including interstitial nephritis, nephrotic syndrome and renal failure.

General disorders and administration site conditions: Malaise, fatigue.

Overdose:

Symptoms: 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, apnoea, diarrhoea and depression of the CNS and respiratory system have also been rarely reported. Disorientation, excitation, fainting and cardiovascular toxicity, including hypotension, bradycardia and tachycardia have 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.

Treatment: Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.

Drug interactions:

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

Antihypertensives, beta-blockers and diuretics: NSAIDs may reduce the effect of anti-hypertensives, such as ACE inhibitors, beta-blockers and diuretics.

Diuretics can also increase the risk of nephrotoxicity of NSAIDs.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels.

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

Lithium: Decreased elimination of lithium.

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

Ciclosporin: Increased risk of nephrotoxicity.

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.

Other analgesics and cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs, including Cox-2 inhibitors, as this may increase the risk of adverse effects.

Aspirin: As with other products containing NSAIDs, concomitant administration of ibuprofen and aspirin is not generally recommended because of the potential of increased adverse effects.

Anticoagulants: NSAIDs may enhance the effects of anticoagulants, such as warfarin.

Quinolone antibiotics: 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.

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

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

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

Aminoglycosides: NSAIDs may decrease the excretion of aminoglycosides.

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

CYP2C9 Inhibitors: Concomitant administration of ibuprofen with CYP2C9 inhibitors may increase the exposure to ibuprofen (CYP2C9 substrate). 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.

Cautions:

Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medication.

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

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin.

When GI bleeding or ulceration occurs in patients receiving Ibuprofen, the treatment should be withdrawn.

NSAIDs should be given with care to patients with a history of ulcerative colitis or Crohn's disease as these conditions may be exacerbated.

Caution is required if Ibuprofen is administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients.

The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. Renal function should be monitored in these patients.

Caution should be used when initiating treatment with ibuprofen in patients with considerable dehydration.

As with other NSAIDs, long-term administration of ibuprofen has resulted in renal papillary necrosis and other renal pathologic changes.

In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis.

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.

Ibuprofen, like other NSAIDs, can interfere with platelet aggregation and has been shown to prolong bleeding time in normal subjects.

Aseptic meningitis 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.

Effects on ability to drive and 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.

Presentation:

Box of 10 film coated tablets of 400 mg (1 blister x 10 film coated tablets) with instruction for use.

Storage:

Keep in dry place, protected from light at a temperature below 25°C.

Keep out of reach of children.

Shelf life:

Labeled. Do not use after expiry date.

Distribution Condition:

Non-prescribed medicine.

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