SPEDIFEN®400

IBUPROFEN ARGININE

美樂芬止痛素 400mg

COMPOSITION

Each sachet contains active ingredient: ibuprofen (as arginine) 400 mg. Excipients: L-arginine, sodium bicarbonate, saccharin sodium, aspartame, apricot flavour, sucrose.

THERAPEUTIC INDICATIONS

For symptomatic relief of pain: such as headache including migraine, toothache, dysmenorrhoea, sign and symptom of rheumatoid arthritis.

DOSAGE AND ADMINISTRATION

Adults:

2-4 sachets/day according to medical advice
The maximum daily dose should not exceed 1600 mg.
The administration should be taken during or after meals.
In elderly the posology must be carefully assessed by the physician since a reduction of the above mentioned dosage may be needed.
The content of each sachet must be dissolved in a glass of water (50-100 ml) and immediately taken.

CONTRAINDICATIONS

Patients who have previously shown hypersensitivity to the components of the drug. Patients with active peptic ulceration or a history of peptic ulceration; active gastrointestinal bleeding; active cerebrovascular bleeding; ulcerative colitis; hemorrhagic diathesis; severe hepatic and/or renal impairment. Severe heart failure (NYHA IV). Since cross reactivity, between aspirin and other non-steroidal anti-inflammatory drugs have been reported, SPEDIFEN® is contraindicated in patients in whom aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) have induced allergic reactions such as asthma, rhinitis, nasal polyps, angioedema. Patients with systemic lupus erythematosus and with collagen diseases must consult the physician before using SPEDIFEN®. SPEDFEN® contains aspartame, thus it is contraindicated in patients suffering from phenylketonuria. The use of ibuprofen during pregnancy and lactation should be avoided.

WARNINGS AND PRECAUTIONS

All NSAIDs (including both COX-2 selective and non-selective NSAIDs) should be prescribed at the lowest effective dose and the duration of treatment should be periodically reviewed and kept as short as possible.

GI Effects

Gastrointestinal bleeding, which is occasionally severe, and peptic ulceration have been reported in some patients receiving ibuprofen. Even if these events are rare, SPEDIFEN® should be given under strict medical supervision to patients with a history of/or with active gastrointestinal tract diseases, such as ulcerative colitis, Crohn's disease.
Serious GI toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated with NSAIDs therapy. Although minor upper GI problems (e.g. dyspepsia) are common, usually developing early in therapy, prescribers should remain alert for ulceration and bleeding in patients treated with NSAIDs even in the absence of previous GI tract symptoms. Studies to date have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Patients with prior history of serious adverse events and other risk factors associated with peptic ulcer disease (e.g. alcoholism, smoking and corticosteroid

therapy) are at increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less than other individuals and account for most spontaneous reports for fatal GI events.

Cardiovascular and Cerebrovascular Effects
Non-selective NSAIDs may be associated with a small increase in the absolute risk of cardiovascular events (e.g. myocardial infarction and stroke), especially when used at high doses for long-term treatment.
Clinical studies suggest that use of ibuprofen, particularly at a high dose (2,400 mg/day), may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1,200 mg/day) is associated with an increased risk of arterial thrombotic events, particularly myocardial infarction. All NSAIDs should be prescribed at the lowest effective dose and the duration of treatment should be periodically reviewed and kept as short as possible.
Patients with uncontrolled hypertension, congestive heart failure, established ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2,400 mg/day) should be avoided. Careful consideration should also be exercised before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2,400 mg/day) are required.
All NSAIDs should not be used perioperatively in patients who have recently undergone coronary artery bypass graft (CABG) surgery and revascularization procedures.

Severe Skin Reactions
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 NSAIDSs. Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment.
Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. SPEDIFEN® should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Other Effects
Caution should be taken for patients with a history of bronchospasm, particularly if it was followed by drugs administration, and in patients with reduced renal and/or hepatic or cardiac functions. In those patients, clinical and laboratory parameters should be periodically monitored especially if prolonged treatment is required.
Caution is required in patients with history of hypertension and/or heart failure, as water retention and oedema have been reported in association with NSAID therapy.
Caution is required in patients with systemic lupus erythematosus or other collagen diseases.
As ibuprofen, like other NSAIDs can prolong the bleeding time, it should be used with caution in patients with intrinsic coagulation defects and in patients on anticoagulant therapy.
Patients who develop ocular disturbances should discontinue the use of SPEDIFEN® and undergo an ophthalmic examination.
Caution should be used when initiating treatment with ibuprofen in patients with considerable dehydration.
Ibuprofen may mask the objective and subjective signs of an infection. In isolated cases an exacerbation of infective inflammations (e.g. development of necrotizing fasciitis) has been described in temporal connection with the use of NSAIDs. Therapy with ibuprofen in patients with an infection should therefore be used with care.
Patients the activity of whom requires surveillance should pay attention if somnolence, dizziness or depression occurs during ibuprofen treatment.

KEEP OUT OF THE REACH OF CHILDREN

INTERACTIONS

- *Acetylsalicylic acid/aspirin:* As with other products containing NSAIDs, concomitant administration of ibuprofen and acetylsalicylic acid/aspirin is not generally recommended because of the potential of increased adverse effects. Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid/aspirin on platelet aggregation when they are dosed concomitantly. Some pharmacodynamics studies show that when single doses of ibuprofen 400 mg were taken within 8 h before or within 30 min after immediate release aspirin dosing (81 mg), a decreased effect of acetylsalicylic acid/aspirin on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid/aspirin cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use.

Diuretics: The efficacy of furosemide, thiazide diuretics or other diuretics can be decreased, probably due to sodium retention related to an inhibition of prostaglandin synthesis in the kidneys.

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding (See warnings and precautions).

Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (See warnings and precautions). The prothrombin time must be carefully monitored during the first weeks of concomitant treatment. Change in the anticoagulant dosage may be required.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (See warnings and precautions).

Anti-hypertensive agents: Ibuprofen may diminish the effect of anti-hypertensives. Consequently, the concomitant use of NSAIDs and ACE-inhibitors or beta-blocking agents may be associated with a risk of acute renal failure. Antagonism of the antihypertensive effect of beta adrenergic blocking agents by NSAIDs has been reported.

Digoxin, phenytoin, lithium: In the literature individual cases of increased plasma levels of digoxin, phenytoin and lithium due to ibuprofen have been described.

Other non-steroidal anti-inflammatory drugs (NSAIDs), including cyclooxygenase-2selective inhibitors:
Ibuprofen (like other NSAIDs) should be used with caution in combination with acetylsalicylic acid or other NSAIDs and systemic corticosteroids: this may increase the risk of adverse drug reactions in the gastro intestinal tract.

Methotrexate: Ibuprofen can increase methotrexate plasma levels.

Zidovudine: Concurrent treatment of zidovudine and ibuprofen can increase the risk of haemarthoses and haematoma in HIV(+) haemophilic patients.

Tacrolimus: Concurrent use of ibuprofen and tacrolimus can increase the risk of nephrotoxicity, due to the reduction of the renal prostaglandins synthesis.

Hypoglycaemic agents: Ibuprofen increases hypoglycemic effect of oral hypoglycemic agents and insulin. It may be necessary to adjust the dosage.

Cyclosporine: Concurrent use of non-steroidal anti-inflammatory drugs (NSAIDs) may result in an increased risk of cyclosporine nephrotoxicity effect.

Voriconazole or Fluconazole: Concurrent use of ibuprofen may result in increased ibuprofen exposure and plasma concentration.

Mifepristone: Concurrent use of non-steroidal anti-inflammatory drugs (NSAIDs) may result in increased exposure to the NSAID.
A decrease in the efficacy of mifepristone can theoretically occur due to the antiprostaglandin properties of NSAIDs.

Quinolone antibiotics: Concurrent use of non-steroidal anti-inflammatory drugs (NSAIDs) may result in an increased risk of seizures.

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

Aminoglycosides: NSAIDs may decrease the excretion of aminoglycosides.

Interactions with diagnostic test results:
- Bleeding time (may prolong bleeding time until 1 day after discontinuation of therapy)
- Serum glucose concentrations (may decrease)
- Creatinine clearance (may decrease)
- Haematocrit or haemoglobin (may decrease)
- BUN, serum creatinine concentrations and kaliemia (may increase)
- Liver function test (may occur elevation of transaminases).

PREGNANCY AND LACTATION
The use of ibuprofen during pregnancy and lactation should be avoided.

Use of NSAIDs at about 20 weeks gestation or later in pregnancy may cause foetal renal dysfunction leading to oligohydramnios and in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation.

SIDE EFFECTS
Effects on the gastrointestinal tract
The most frequent adverse effects occurring with ibuprofen are gastrointestinal disturbances: heartburn, anorexia, nausea, vomiting, dyspepsia, gastric pyrosis, abdominal discomfort, diarrhoea, ulcer activation and gastrointestinal bleeding.

Effects on the central nervous system
Headache, confusion, tinnitus and somnolence have been reported less frequently than gastrointestinal effects.
Cases of psychotic and depressive reactions were experienced.
Individual cases of severe headache, nausea, vomiting, fever, stiffness of neck muscles, sensorial disturbance (earlier sign of meningitis) were experienced.

Effects on sense organs
Reversible ocular reactions were observed: toxic amblyopia, blurred vision and changes in colour vision.

Effects on the skin/hypersensitivity reactions

Skin rashes, including urticaria, exanthema and purpura were reported. Those reactions may be accompanied with pruritus and Stevens-Johnson's syndrome.
General reactions of hypersensitivity may be rarely experienced. Symptoms may be fever with skin rashes, abdominal pain, headache, nausea and vomiting, abnormalities of liver function tests, meningism and anaphylactic reactions.
Systemic Lupus Erythematosus or other collagenous disease can increase the risk of general hypersensitivity reactions.
Rarely, ibuprofen may induce bronchospasm in predisposed patients.

Effects on the blood
Doses higher than 1000 mg/day can prolong the bleeding time. Blood alterations have been reported with differences both in nature and in severity: thrombocytopenia, granulocytopenia, agranulocytosis, haemolytic anaemia and aplastic anaemia. Such blood dyscrasias have been observed particularly alter prolonged administration of high doses.

Effects on the liver
Abnormalities of liver function tests (high levels of serum transaminases) and icterus have been reported. Hepatic disorder, liver injury, hepatitis, Jaundice.
See also hypersensitivity reactions.

Effects on the kidneys
Sodium and water retention and oedema have been reported. Cases of dysuria and of acute intestinal nephritis have been experienced. Impaired renal functions may be experienced with different severity, particularly alter prolonged administration of high doses. Acute renal failure may occur in case of general hypersensitivity reactions.
Cases of renal injury (renal papillary necrosis) have been reported.

Other undesirable effects
Stomatitis, menstrual disorder, increased serum levels of urates have been occasionally experienced.
In case that adverse events occur, treatment must be immediately suspended and the physician must be consulted.DO NOT USE THE PRODUCT AFTER THE EXPIRY DATE REPORTED ON THE PACKAGING.
The reported expiry date is referred to the product in the original packaging and properly stored.

SYMPTOMS AND TREATMENT OF OVERDOSE
Gastric lavage and, if it is necessary, correction of serum electrolytes.
There is no specific antidote for ibuprofen.

PACKAGING
SPEDIFEN® 400 - 30 sachets

MANUFACTURER:
Zambon Switzerland Ltd., 6814 Cadempino, Switzerland

Revision of the package: December 2021