SPIDIFEN 400 mg Film-coated tablets

Ibuprofen arginine salt

PHARMACOTHERAPEUTIC GROUP
Non-steroidal antirheumatic, anti-inflammatory drugs.

THERAPEUTIC INDICATIONS
Treatment of pain: headache, toothache, period pains, neuralgia, joint and muscle pains, episiotomy and post-partum pain, pain following tooth extraction, postoperative pain, pain from small injuries or traumatisms.
Forms of inflammatory rheumatism: rheumatoid arthritis, ankylosing spondylitis, STILL's disease.
Forms of degenerative rheumatism: osteoarthrosis (cervical, dorsal, lumbar arthrosis, gonarthrosis, coxarthrosis, polyarthrosis, etc.).
Extra-articular rheumatic forms: tendinitis, fibrositis, bursitis, myalgia, lumbago, scapulohumeral periarthritis, ischialgia, radiculoneuritis.

CONTRAINDICATIONS
- Hypersensitivity to the active ingredient or to other strictly related chemical substances and/or to any of the excipients.
- History of gastrointestinal bleeding or perforation, related to previous active treatments or history of bleeding//recurrent peptic ulcer (two or more different episodes of ascertained ulceration or bleeding).
- Active and recurrent peptic ulcer.
- Ongoing gastrointestinal bleeding.
- Ulcerative colitis and Crohn's disease.
- Severe hepatic and/or renal failure.
- Severe heart failure.
  Owing to the possible risk of allergic cross-reactions with acetylsalicylic acid or other non-steroidal anti-inflammatory drugs, the product is contraindicated in patients who after use of the mentioned drugs develop allergic reactions, such as asthma, urticaria, rhinitis, nasal polyposis, angioedema. In the presence of systemic lupus erithematosus and collagen diseases, it is necessary to consult the attending physician before using SPIDIFEN.
- Third trimester of pregnancy.

PRECAUTIONS FOR USE
Concomitant use of SPIDIFEN and NSAIDs, including COX-2 selective inhibitors should be avoided.
Undesirable effects can be minimized by using the lowest effective dose for the shortest possible time necessary to relieve symptoms.
Elderly patients: elderly patients may be exposed to a higher frequency of NSAID-related adverse reactions, especially gastrointestinal bleeding and perforation, sometimes with fatal outcome (see section "Dose, method and time of administration").
Gastrointestinal bleeding, ulceration and perforation: gastrointestinal bleeding, ulceration and perforation, which may be fatal, have been reported with all NSAIDs, at any time during treatment, with or without warning symptoms or previous history of serious gastrointestinal events.
In elderly patients and in patients with history of ulcer, particularly if complicated by bleeding or perforation (see section "Contraindications"), the risk of gastrointestinal bleeding, ulceration or perforation is higher with increased NSAID doses. These patients should therefore start the treatment at the lowest available effective dose. The concomitant use of protective agents (misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients receiving low aspirin

doses or other medicines which may increase the risk of gastrointestinal events (see below and section "Interactions").
Patients with a history of gastrointestinal toxicity, in particular elderly patients, should report any unusual gastrointestinal symptoms (especially gastrointestinal bleeding), particularly at the initial stages of treatment.
At daily doses higher than 1000 mg ibuprofen may prolong the bleeding time.
Caution is required 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 antiplatelet agents such as aspirin (see section "Interactions").
When gastrointestinal bleeding or ulceration occurs in patients receiving SPIDIFEN, the treatment should be withdrawn.
NSAIDs should be administered with caution in patients with history of gastrointestinal disease (ulcerative colitis, Crohn's disease), as these conditions may be exacerbated (see section "Possible side effects").
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.
Severe cutaneous reactions, some of which possibly fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, were very rarely associated with NSAIDs use (see section "Possible side effects"). Patients appear to be more at risk during the first stages of therapy: reactions occur in most cases within the first month of treatment. SPIDIFEN should be discontinued upon the first onset of skin rash, mucosal injuries or any other hypersensitivity signs.
Hepatotoxic reactions may occur within a picture of generalized hypersensitivity reactions.
Caution should be exercised when treating patients with previous episodes of bronchospasm, especially following the use of other drugs, and with impaired renal and/or hepatic or cardiac function. Such patients require a regular monitoring of clinical and laboratory parameters, especially in case of prolonged treatment.
Systemic lupus erythematosus or other collagen diseases represent risk factors for severe manifestations of generalized hypersensitivity.
Since eye alterations have been reported, though very rarely, during ibuprofen treatment, it is recommended, in case of visual disorders, to discontinue the treatment and perform an ophthalmologic examination.

INTERACTIONS
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicine, including medicines obtained without a prescription.
Some medicines, such as anticoagulants and antiplatelet drugs (eg. acetylsalicylic acid/warfarin, ticlopidine), antihypertensive agents (ACE-inhibitors, such as captopril, beta-blockers, angiotensin II antagonists) and other drugs may interact with ibuprofen treatment.
Ask your doctor before using ibuprofen with other medicines.
Diuretics, ACE –inhibitors and angiotensin II antagonists:
NSAIDs may reduce the efficacy of diuretics and other antihypertensive agents. In some patients with impaired renal function (for example dehydrated patients or elderly patients with impaired renal function), the co-administration of an ACE inhibitor or an angiotensin II antagonist as well as cyclooxygenase inhibitors, may lead to a further deterioration of the renal function, including a possible, usually reversible, acute renal failure. These interactions should be taken into account in patients taking SPIDIFEN concomitantly with ACE inhibitors or angiotensin II antagonists. Therefore the combination should be administered with due caution, especially in elderly patients.
Patients should be appropriately hydrated and monitoring of renal function should be considered after initiation of concomitant therapy.
Corticosteroids: increased risk of ulceration or gastrointestinal bleeding (see section "Precautions for use").
Anticoagulants: NSAIDs may increase the effects of anticoagulants, such as warfarin (see section "Precautions for use"). Prothrombin time should be carefully controlled during the first weeks of combined treatment, and anticoagulant dose adjustment may be required.

Antiplatelet drugs and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see section “Precautions for use”).
A reduction in thiazide diuretics efficacy may occur, probably due to sodium retention associated with prostaglandin synthetase inhibition at renal level.
The hypotensive effect of beta-blockers may be reduced.
The association with aspirin or other NSAIDs should be avoided, as ibuprofen may reduce the cardioprotective effect of acetylsalicylic acid when taken concomitantly.
Isolated cases of high digoxin, phenytoin and lithium plasma levels are reported in literature, resulting from ibuprofen-combined therapy.

SPECIAL WARNINGS
Medicines like SPIDIFEN may be associated with a slightly increased risk of heart attack (“myocardial infarction”) or stroke. Whatever risk is more probable with high doses and prolonged treatments. Do not exceed the recommended dose or the treatment duration.
If you have heart problems, or have experienced stroke in the past or think you may be at risk for these conditions (for instance if you suffer from high blood pressure, diabetes or high cholesterol level or if you are a smoker) you should discuss the therapy with your doctor or pharmacist.

Driving and using machines
SPIDIFEN may impair the ability to drive and use machines, due to the possible onset of somnolence, dizziness or depression.
Due caution is needed for those patients whose activity requires particular alertness, should they experience somnolence, dizziness or depression during ibuprofen therapy.

Pregnancy and breast-feeding
SPIDIFEN is contraindicated during the third trimester of pregnancy. SPIDIFEN should not be administered during the first and second trimester of pregnancy, unless in cases of strict necessity.
Should SPIDIFEN be used in a woman who wish to conceive or during the first and second trimester of pregnancy, dose and treatment duration should be as low as possible.
SPIDIFEN administration should be withdrawn in women with fertility problems. Moreover, the product use is not recommended during lactation and in childhood.

Important information about some of the ingredients of SPIDIFEN
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
SPIDIFEN contains 82.62 mg of sodium. This should be taken into account in case of low-sodium regimens.

DOSE METHOD AND TIME OF ADMINISTRATION
The product use is intended for adult patients only.
The posology is 2-4 tablets daily, according to medical advice.
The maximum daily dose should not exceed 1800 mg. Within the rheumatology field, in order to improve the morning joint stiffness, it is recommended to administer the first daily dose upon the patient’s awakening, and the subsequent ones during or after meals.
In the treatment of elderly patients, the posology should be carefully established by the doctor, who has to consider a possible reduction in the above mentioned dosages.

OVERDOSE
In case of accidental ingestion/administration of an excessive dose of SPIDIFEN, contact your doctor or the nearest hospital immediately.
Most cases of overdose are asymptomatic. The main symptoms, when present, are of moderate intensity and include abdominal pain, nausea, vomiting, lethargy, somnolence, headache, tinnitus and ataxia. The most serious manifestations include apnoea, acute respiratory insufficiency, metabolic acidosis, coma,

seizures, acute renal failure, rhabdomyolisis, hypotension and hypothermia. The onset of the symptomatology is generally observed within 4 hours of overdose.
In case of overdose, gastrolavage and serum electrolyte adjustment are indicated.
There is no specific antidote for ibuprofen. In case of NSAID overdose, patients should receive symptomatic and support treatments. Given the high plasma protein binding of ibuprofen (up to 99%), it is unlikely that dialysis could be useful in case of overdose, similarly to forced diuresis and urine alkalinization. Renal and hepatic function should be monitored.

If you have any further questions on the use of SPIDIFEN, ask your doctor or pharmacist.

POSSIBLE SIDE EFFECTS
Like all medicines, SPIDIFEN may cause side effects, although not everybody gets them.
The most commonly reported adverse events affect the gastrointestinal tract. Peptic ulcer, gastrointestinal perforation or gastrointestinal bleeding, sometimes with fatal outcome, may occur, particularly in elderly subjects (see section “Special warnings”).
After SPIDIFEN administration, the following symptoms have been reported: nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, gastric pyrosis, melaena, haematemesis, ulcerative stomatitis, colitis and Crohn’s disease exacerbation (see section “Special warnings”). Gastritis was reported less frequently.
Oedema, hypertension and heart failure have been reported in association with NSAID treatment.
Medicines like SPIDIFEN may be associated with a slightly increased risk of heart attack (“myocardial infarction”) or stroke.
Anorexia, headache, confusion, tinnitus and somnolence occur with a lower frequency with respect to gastrointestinal effects.
Cases of psychotic reaction and depression have been reported.
In single cases ibuprofen administration was followed by high-intensity headache, nausea, vomiting, fever, neck stiffness, clouded sensorium (initial signs of meningitis).
Reversible effects on eyes have been observed, such as toxic ambliopia, blurred vision, altered colour perception.
Various types of skin rash, including urticaria, exanthem and purpura, associated or not with itching, bullous reactions including Stevens-Johnson syndrome and Toxic Epidermal Necrolysis (very seldom) were reported.
Hypersensitivity generalized reactions occur unfrequently. Symptoms may include fever associated with skin rash, abdominal pains, headache, nausea and vomiting, signs of hepatic dysfunction and also meningism and anaphylactic phenomena.
Systemic lupus erythematosus or other collagen diseases represent risk factors for severe manifestations of generalized hypersensitivity.
In rare cases ibuprofen may induce bronchospasm in predisposed patients.
At daily doses exceeding 1000 mg ibuprofen may prolong the bleeding time. Alterations of various nature and severity affecting the corpuscolate component of the blood have been reported, such as: trombocytopenia, granulocytopenia, agranulocytosis, haemolytic anaemia and aplastic anaemia.
These blood dyscrasias occur particularly after prolonged administration of high dosages.
Cases of hepatic function alterations (high levels of serum transaminases) and jaundice were reported.
Hepatotoxic reactions may occur within a picture of generalized hypersensitivity reactions.
Cases of sodium and water retention or oedema are known. Reports of dysuria and acute interstitial nephritis were received. Renal failure may occur with varying degrees of severity, in particular after prolonged administration of high dosages.
Acute renal failure may appear in case of generalized hypersensitivity reaction. In addition, reports of renal damage are known (papillary necrosis).
Occasionally menstrual irregularities and increased serum urate levels were reported.

The onset of undesirable effects during treatment requires immediate therapy withdrawal and medical advice.
If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

EXPIRY DATE AND STORAGE
Film-coated tablets should be stored at a temperature not exceeding 30°C.
KEEP OUT OF THE REACH OF CHILDREN

ATTENTION: DO NOT USE THIS MEDICINE AFTER THE EXPIRY DATE WHICH IS STATED ON THE CARTON
This date refers to the product in the original packaging and properly stored.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

SHELF LIFE
3 years

COMPOSITION

One 400 mg tablet contains: **Active ingredient**: ibuprofen arginine salt, equal to ibuprofen 400 mg
Excipients: l-arginine, sodium bicarbonate, crospovidone, magnesium stearate, hydroxypropylmethylcellulose, sucrose, titanium dioxide, polyethylene glycol.

PHARMACEUTICAL FORM AND PACKAGES
400 mg film-coated tablets – 12 and 30 tablets

M.A. HOLDER: ZAMBON S.p.A. - Via Lillo del Duca 10 - 20091 Bresso (MI)
MANUFACTURER RESPONSIBLE FOR BATCH RELEASE:
ZAMBON S.p.A. - Via della Chimica 9 - Vicenza

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