

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen Strides 600 mg filmomhulde tabletten

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 600 mg ibuprofen

Excipient with known effect:

Each 600mg film-coated tablet contains 2.40 mg lactose (as monohydrate).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Ibuprofen Strides 600 mg: White colored oval shaped biconvex film coated tablets debossed '6' on one side and break line on other side and a length of approx. 17.7 mm and a width of approx. 10.6 mm.

The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Adults and adolescents from 15 years of age (≥ 50 kg)

Symptomatic treatment of pain and inflammation in arthritic diseases (e.g. rheumatoid arthritis), degenerative arthritic conditions (e.g. osteoarthritis), and in painful swelling and inflammation after soft tissue injuries.

4.2 Posology and method of administration

Posology

The ibuprofen dose depends on patient's age or body weight.

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms (see section 4.4).

Rheumatic diseases and painful swelling and inflammation after soft tissue injuries

Adults and adolescents from 15 years (≥ 50 kg):

The single dose is 300-600 mg ibuprofen. The recommended daily dose is 1200-1800 mg ibuprofen in divided doses. An interval of at least 6 hours should be allowed between doses. Some patients can be maintained on 600-1200 mg daily. In severe or acute conditions, it can be advantageous to increase the dose until the acute phase is brought under control, provided the total daily dose does not exceed 2400 mg in divided doses.

The duration of treatment is determined by the treating physician.

For rheumatic diseases, it may be necessary to take Ibuprofen Strides over a prolonged period of time.

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.

Renal impairment

Caution should be taken in patients with mild to moderate renal impairment. The dose should be kept as low as possible and renal function should be monitored (see section 4.4). The medicinal product is contraindicated in patients with severe renal impairment (see section 4.3)

Hepatic impairment

Caution should be taken in patients with mild to moderate hepatic impairment. The dose should be kept as low as possible (see section 4.4). The medicinal product is contraindicated in patients with severe hepatic impairment (see section 4.3).

Pediatric population

Ibuprofen Strides 600 mg film-coated tablets are not indicated in adolescents below 50 kg body weight or in children or adolescents younger than 15 years.

Method of administration

Ibuprofen Strides tablets are for oral use and should be taken with a glass of water.

People with a sensitive stomach are advised to take Ibuprofen Strides tablets with some food.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- History of hypersensitivity reactions (e.g. bronchospasm, asthma, urticaria, angioedema or rhinitis) associated with the intake of acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs).
- Active or a history of recurrent peptic ulcer/bleeding (two or more clear distinct of proven ulceration or bleeding).
- Severe hepatic impairment.
- Severe heart failure (NYHA Class IV)
- Severe renal impairment
- History of gastrointestinal bleeding or perforation associated with previous NSAIDs therapy.
- Cerebrovascular or other active bleeding.
- Unclassified blood-formation disturbances.
- Conditions involving an increased tendency to bleeding
- Severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake)
- The third trimester of pregnancy (see section 4.6).
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4.4 Special warnings and precautions for use

General precautions

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and gastrointestinal and cardiovascular effects below).

On prolonged use of any painkillers, headache may occur that must not be treated with increased doses of the medicinal product.

Through concomitant consumption of alcohol, active substance-related undesirable effects, particularly those that concern the gastrointestinal tract or the central nervous system, may be increased on use of NSAIDs.

In general, habitual intake of analgesics, particularly a combination of several analgesic medicinal products, may lead to permanent renal damage with the risk of renal failure (analgesic nephropathy). This risk may be increased under physical strain associated with loss of salt and dehydration.

During prolonged use of ibuprofen regular monitoring of liver function tests, renal function and blood counts is required.

Caution is required in patients:

- with systemic lupus erythematosus or mixed connective tissue disease (see section 4.8)
- with congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria)
- with gastrointestinal disorders and bowel inflammations (ulcerative colitis, Crohn's disease)
- with hypertension and/or heart problems
- with renal disorders
- with impaired liver function
- immediately after major surgery
- with dehydration
- who have had hypersensitivity or allergic reactions to other substances, as they could be at an increased risk of hypersensitivity reactions with Ibuprofen Strides
- who suffer from hay fever, nasal polyps or chronic obstructive respiratory disorders, as for them an increased risk of allergic reactions exists. These may present as asthma attacks (so-called analgesic asthma), Quincke's oedema or urticaria.

Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed very rarely. At the first signs of hypersensitivity reaction after taking Ibuprofen Strides, therapy must be stopped. Medically required measures, in line with the symptoms, must be initiated by specialist personnel.

Respiratory disorders

Bronchospasm may be precipitated in patients suffering from, or with a history of, bronchial asthma or allergic disease.

Cardiovascular and cerebrovascular effects

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 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. \leq 1200 mg/day) is associated with an increased risk of arterial thrombotic events.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 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, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

Cases of Kounis syndrome have been reported in patients treated with Ibuprofen Strides. Kounis syndrome has been defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to myocardial infarction.

Gastrointestinal effects

The concomitant administration of ibuprofen and other NSAIDs, including selective

cyclooxygenase-2 (COX-2) inhibitors should be avoided.

Elderly patients

Elderly patients are at greater risk of experiencing undesirable effects when treated with an NSAID, especially gastrointestinal bleeding and perforation, which may be fatal.

Gastrointestinal bleeding, ulceration and perforation

Gastrointestinal bleeding, ulceration and perforation, which can 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.

The risk of gastrointestinal bleeding, ulceration or perforation is higher with increasing NSAIDs doses, in patients with a history of ulcer, especially if complicated with bleeding or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available.

Combination therapy with protective active substances (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose acetylsalicylic acid, or other medicinal products likely to increase gastrointestinal risk (see below and 4.5).

Patients with a history of gastrointestinal toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially GI bleeding), particularly in the initial stages of treatment. Caution should be advised in patients receiving concomitant medication which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin re-uptake inhibitors or antiplatelet medicine such as acetylsalicylic acid (see section 4.5).

Treatment with ibuprofen should be withdrawn if the patient suffers from gastrointestinal bleeding or ulceration.

NSAIDs should be given with caution to patients with a history of gastrointestinal disease, e.g. ulcerative colitis and Crohn's disease, as these conditions may be exacerbated (see section 4.8).

Renal effects

Caution should be taken in patients with mild to moderate renal impairment as renal function may further deteriorate (see sections 4.2 and 4.8). There is a risk of renal impairment especially in dehydrated adolescents and elderly.

Haematological effects

Ibuprofen can temporarily inhibit platelet aggregation (thrombocyte aggregation). Patients with coagulation disturbances should therefore be carefully monitored.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome), and acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with the use of ibuprofen (see section 4.8). Most of these reactions occurred within the first month.

If signs and symptoms suggestive of these reactions appear ibuprofen should be withdrawn immediately and an alternative treatment considered (as appropriate).

Infections and infestations

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissues infectious complications.

To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of Ibuprofen Strides in case of varicella.

Masking of symptoms of underlying infections

Ibuprofen can mask symptoms of infection, which may lead to delayed initiation of appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to varicella. When Ibuprofen Strides is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In nonhospital settings, the patient should consult a doctor if symptoms persist or worsen.

Aseptic meningitis

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.

Patients with gastrointestinal problems, SLE, haematological or coagulation disorders and asthma should be treated with caution and be closely monitored during NSAID treatment, since their condition may be exacerbated by the NSAID.

Paediatric population

There is a risk of renal impairment in dehydrated adolescents.

Information related to excipients

This medicinal product contains lactose (as monohydrate). Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen should only be taken with caution together with the following active substances:

Other NSAIDs including salicylates: Concomitant use of several NSAIDs can increase the risk of gastrointestinal ulcers and bleeding due to a synergistic effect. Concomitant use of ibuprofen with other NSAIDs should therefore be avoided (see section 4.4).

Selective inhibitors of cyclooxygenase-2: The concomitant administration of ibuprofen with other NSAIDs, including selective inhibitors of cyclooxygenase-2 should be avoided due to the potential additive effect (see section 4.4).

Acetylsalicylic acid: Concomitant administration of ibuprofen and acetylsalicylic acid 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 on platelet aggregation when they are dosed concomitantly. 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 cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

Mifepristone: If NSAIDs are used within 8-12 days after mifepristone administration they can reduce the effect of mifepristone.

Sulphonylureas: There are rare reports of hypoglycaemia in patients on sulphonylurea medications receiving ibuprofen. A check of blood glucose values is recommended as precaution on concomitant intake.

Zidovudine: There is evidence of an increased risk of haemarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Ritonavir: May increase the plasma concentrations of NSAIDs.

Aminoglycosides: NSAIDs may reduce the excretion of aminoglycosides.

ACE inhibitors, angiotensin-II antagonists and diuretics:

Non-steroidal anti-inflammatory drugs can attenuate the effect of diuretics and antihypertensives. Diuretics may also increase the NSAIDs nephrotoxicity risk. In patients with impaired renal function (e.g. dehydrated patients or elderly patients with impaired renal function), concomitant intake of an ACE inhibitor, beta-receptor blocker or angiotensin-II antagonist with a cyclooxygenase inhibitor can lead to further deterioration of renal function, including possible acute renal failure, which is usually reversible. Hence, such a combination should only be used with caution, particularly in elderly patients. Patients must be instructed to maintain adequate fluid intake and regular monitoring of kidney function tests should be considered upon initiation of combination therapy.

Co-administration of ibuprofen and potassium-sparing diuretics can lead to hyperkalaemia (check of serum potassium is recommended).

Beta-blockers: NSAIDs counteract the antihypertensive effect of beta-adrenoceptor blocking medicine.

Digoxin, phenytoin, lithium: Concomitant use of ibuprofen with digoxin, phenytoin or lithium preparations can increase the serum level of these medicinal products. Monitoring of serum-lithium is necessary, monitoring of serum-digoxin and serum-phenytoin levels is recommended.

Quinolone antibiotics: Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

Cyclosporine: The concomitant administration of NSAIDs and cyclosporine is thought to be capable of increasing the risk of nephrotoxicity due to decreased synthesis of prostacyclin in the kidney.

Accordingly, in the event of combination treatment, renal function must be monitored closely.

Captopril: Experimental studies indicate that ibuprofen counteracts the effect of captopril on sodium excretion.

Colestyramine: The concomitant administration of ibuprofen and colestyramine retards and reduces (by 25%) the absorption of ibuprofen. These medicine should be given with at least two hours interval between them.

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

Methotrexate: NSAIDs may inhibit the tubular secretion of methotrexate and reduce its clearance. Administration of ibuprofen within 24 hours before or after methotrexate administration can lead to increased concentration of methotrexate and an increase in its toxic effect.

Anticoagulants: NSAIDs may enhance the effects of anticoagulants, such as warfarin (see section 4.4).

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding with NSAIDs (see section 4.4).

Platelet aggregation inhibitors and selective serotonin reuptake inhibitor (SSRIs): Increased risk of gastrointestinal bleeding (see section 4.4).

Probenecid and sulfinpyrazone: Medicinal products that contain probenecid or sulfinpyrazone may delay the excretion of ibuprofen.

Alcohol, bisphosphonates and oxpentifylline (pentoxifylline): May potentiate the GI side-effects and the risk of bleeding and ulceration.

Baclofen: Elevated baclofen toxicity.

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). In a study with voriconazole and fluconazole (CYP2C9 inhibitors) an increased S(+)-ibuprofen exposure by approximately 80 to 100% has been shown. 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo/foetal development.

Data from epidemiological studies raise concern about an increased risk of miscarriage and of cardiac malformation and gastroschisis after the use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk of cardiovascular malformation was increased from less than 1% up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy. In animals the administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation losses and embryo/foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have also been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. From the 20th week of pregnancy onward, ibuprofen use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimesters of pregnancy, Ibuprofen Strides should not be given unless clearly necessary. If Ibuprofen Strides is used by a woman attempting to conceive or during the first and second trimester, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to ibuprofen for several days from gestational week 20 onward. Ibuprofen Strides should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- Cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension),
- Renal dysfunction (see above).

The mother and the neonate, at the end of pregnancy, to:

- Possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
- Inhibition of uterine contractions, resulting in delayed or prolonged labour.

Consequently Ibuprofen Strides is contraindicated during the third trimester of pregnancy (see sections 4.3 and 5.3).

Breast-feeding

Ibuprofen is excreted in breast milk, but with therapeutic doses during short term treatment the risk for influence on infant seems unlikely. If, however, longer treatment is prescribed, early weaning should be considered.

Fertility

The use of ibuprofen may impair fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of ibuprofen should be considered.

There is some evidence that drugs which inhibit cyclo-oxygenase/ prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

4.7 Effects on ability to drive and use machines

Ibuprofen generally has no or negligible influence on the ability to drive and use machines. However, since at higher dose central nervous undesirable effects such as tiredness and dizziness may occur, the ability to react and the ability to take part actively in road traffic and to operate machines may be impaired in individual cases. This applies to a greater extent in combination with alcohol.

4.8 Undesirable effects

It must be remembered that the following adverse drug reactions are mainly dose dependent and vary between individuals.

Gastrointestinal: The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, melena, hematemesis, ulcerative stomatitis, and exacerbation of colitis and Crohn's disease (see section 4.3) have been reported following administration. Less frequently, gastritis has been observed.

Clinical studies suggest that use of ibuprofen particularly at a high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke, see section 4.4).

Oedema, hypertension and heart failure have been reported in connection with NSAID treatment.

The following categories are used for expressing the frequency of adverse reactions: Very common ($\geq 1/10$), Common ($\geq 1/100$ to $< 1/10$), Uncommon ($\geq 1/1000$ to $< 1/100$), Rare ($\geq 1/10,000$ to $< 1/1000$), Very rare ($< 1/10,000$) and Not known (cannot be estimated from the available data).

System organ class	Frequency	Undesirable effects
Infections and Infestations	Very rare	<p>Exacerbation of infection-related inflammation (e.g. development of necrotising fasciitis) has been described in temporal association with the systemic use of non-steroidal anti-inflammatory drugs. This is possibly associated with the mechanism of action of non-steroidal anti-inflammatory drugs.</p> <p>The patient should be advised to consult a physician immediately, if signs of infection appear or deteriorate during the use of Ibuprofen Strides. It should be checked whether there is an</p>

		<p>indication for anti-infective/antibiotic therapy.</p> <p>Symptoms of aseptic meningitis with neck stiffness, headache, nausea, vomiting, fever or clouding of consciousness on ibuprofen have been reported. Patients with autoimmune disorders (SLE, mixed connective tissue disease) appear to be predisposed</p>
Blood and Lymphatic System Disorders	Very rare	<p>Haematopoietic disorders (anaemia, leukopenia, thrombocytopenia, pancytopenia, agranulocytosis). eosinophilia, coagulopathy (changes in coagulation), aplastic anemia, hemolytic anemia, neutropenia</p> <p>First signs are: fever, sore throat, superficial oral ulcerations, flu like symptoms, extreme fatigue, unexplained bleeding and bruising.</p>
Immune System Disorders	Uncommon	Hypersensitivity with skin rash and itching, as well as asthma attacks (possibly with a drop in blood pressure).
	Very rare	Severe general hypersensitivity reactions. These may manifest as: swelling of the face, tongue and throat, dyspnoea, tachycardia, and drop in blood pressure up to a life-threatening shock.
Metabolism and nutrition disorders	Very rare	<p>Hypoglycemia</p> <p>Hyponatremia</p>
Psychiatric Disorders	Very rare	Psychotic reactions, hallucinations, confusion, depression, anxiety
Nervous System Disorders	common	Disorders of the CNS, such as headache, dizziness, insomnia, agitation, irritability or fatigue
	Very rare	paraesthesia, optic neuritis
Eye Disorders	Uncommon	Visual disorders
Ear and Labyrinth Disorders	Rare	Tinnitus, loss of hearing
Cardiac Disorders	Very rare	Palpitations, heart failure and myocardial infarction
	Not known	Kounis syndrome
Vascular Disorders	Very rare	Arterial hypertension, vasculitis
Respiratory, thoracic and mediastinal disorders	Very rare	Asthma, dyspnea, bronchospasm
	Not known	rhinitis
Gastrointestinal Disorders	Very common	Gastrointestinal symptoms such as pyrosis, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation, and minor gastrointestinal bleeding, which may cause anaemia in exceptional cases.
	Common	Gastrointestinal ulceration, potentially with bleeding and perforation. Ulcerative stomatitis, exacerbation of colitis and Crohn's Disease (see section 4.4), gastritis
	Very rare	Oesophagitis, pancreatitis, formation of intestinal diaphragm -like strictures.
Hepatobiliary Disorders	Very rare	hepatic dysfunction, liver damage, especially during long-term therapy, liver failure, acute hepatitis, jaundice
Skin and Subcutaneous Tissue Disorders	Very rare	Severe cutaneous adverse reactions (SCARs) (e.g. Erythema multiforme, exfoliative dermatitis, bullous reactions including Stevens-Johnson Syndrome, and toxic epidermal necrolysis (Lyell's syndrome)), in exceptional cases severe skin infections

		and soft-tissue complications may occur during a varicella infection (see also “Infections and infestations”), <u>purpura, alopecia</u>
	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), Acute generalised exanthematous pustulosis (AGEP), Photosensitivity reactions
Renal and urinary Disorder	Rare	Renal tissue damage (papillary necrosis, elevated uric acid blood concentrations, elevated urea concentration in the blood.
	Uncommon	Oedema, particularly in patients with arterial hypertension or renal failure, nephrotic syndrome, interstitial nephritis which may be combined with acute renal failure. Regular monitoring of the renal function is therefore required.
	Not known	impaired renal function

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V

4.9 Overdose

Symptoms

Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely, diarrhoea. Nystagmus, blurred vision, tinnitus, headache and gastrointestinal bleeding may also occur. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as vertigo, dizziness, drowsiness, occasionally excitation and disorientation, loss of consciousness or coma. Occasionally patients develop convulsions. Children may also develop myoclonic cramps. In serious poisoning metabolic acidosis may occur, hypothermia and hyperkalaemia may also occur and the prothrombin time/INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure, liver damage, hypotension, respiratory depression and cyanosis may occur. Exacerbation of asthma is possible in asthmatics.

Treatment

There is no specific antidote.

Symptomatic and supportive treatment is therefore indicated in case of overdose. Particular attention is due to the control of blood pressure, acid-base balance and any gastrointestinal bleeding.

Within one hour of ingestion of a potentially toxic amount, the administration of activated carbon should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a life-threatening overdose.

Adequate diuresis should be ensured and renal and hepatic functions should be closely monitored. The patient should remain under observation for at least four hours after ingestion of a potentially toxic amount of medication.

Any onset of frequent or prolonged seizures should be treated with intravenous diazepam. Depending on the patient's clinical condition, other supportive measures may be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, nonsteroids; propionic acid derivatives.

ATC code: M01AE01

Mechanism of action

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID), which has been shown to be effective through inhibition of prostaglandin synthesis in the usual animal models of inflammation. In humans, ibuprofen reduces inflammation-induced pain, swelling and fever. Furthermore, ibuprofen reversibly inhibits ADP- and collagen-induced platelet aggregation.

Clinical efficacy and safety

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400 mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of acetylsalicylic acid 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 cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5).

5.2 Pharmacokinetic properties

Absorption and Distribution

Ibuprofen is well absorbed from the gastrointestinal tract, is extensively bound to plasma protein and diffuses into the synovial fluid. Ibuprofen is more rapidly absorbed from the gastrointestinal tract following administration in the form of sodium salt versus a tablet containing ibuprofen acid (35 minutes vs. 1-2 hours).

Biotransformation

Ibuprofen is metabolised in the liver to two major metabolites, with primary excretion via the kidneys – either as such or as major conjugates – together with a negligible amount of unchanged ibuprofen. Excretion by the kidneys is both rapid and complete.

Elimination

Elimination half-life is approximately 2 hours.

No significant differences in the pharmacokinetic profile are observed in the elderly.

5.3 Preclinical safety data

The sub chronic and chronic toxicity of ibuprofen in animal experiments was observed principally as lesions and ulcerations in the gastro-intestinal tract. *In vitro* and *in vivo* studies gave no clinically relevant evidence of a mutagenic potential of ibuprofen. In studies in rats and mice no evidence of carcinogenic effects of ibuprofen was found. Ibuprofen led to inhibition of ovulation in rabbits as well as disturbance of implantation in various animal species (rabbit, rat, mouse). Experimental studies have demonstrated that ibuprofen crosses the placenta, for maternally toxic doses, an increased incidence of malformations (e.g. ventricular septal defects) was observed.

Ibuprofen poses a risk to the aquatic environment (see section 6.6)

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core

Silica colloidal anhydrous
Cellulose, microcrystalline
Starch, pregelatinised (maize)
Sodium Starch Glycolate
Talc
Magnesium stearate

Tablet Coating

Hypromellose
Titanium Dioxide (E171)
Lactose Monohydrate
Macrogol
Sodium citrate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC-Aluminium Blister containing 10, 20, 30, 40, 50, 60, 70, 80, 90 and 100 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

This medicinal product poses a risk to the environment (see section 5.3). Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Strides Pharma (Cyprus) Limited
Themistokli Dervi, 3
Julia House, 1st Floor
Nicosia 1066
Cyprus

8 MARKETING AUTHORISATION NUMBER

RVG 126783

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 20 februari 2024.

10 DATE OF REVISION OF THE TEXT

