SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen Lysine 342 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains the active ingredient ibuprofen 200 mg (as ibuprofen lysine 342 mg).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.
White to Off-white, film-coated, capsule-shaped tablet, imprinted with “S4” in black on one face.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Short-term symptomatic relief of headache and migraine.

4.2 Posology and method of administration

Posology

Adults and adolescents ≥40 kg (12 years of age and above):
Take 1 or 2 tablets (342 mg or 684 mg) with water, up to three times a day as required. Leave at least six hours between doses.
Do not take more than 6 tablets (2052 mg) in any 24 hour period.
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms. The patient should consult a doctor if symptoms worsen, or if the product is required for more than 5 days (3 days in case of migraine).

Special patient groups

Paediatric population:
Ibuprofen Lysine 342 mg film-coated tablets is contraindicated in adolescents weighing under 40 kg or children under 12 years of age (see section 4.3).

Elderly:
No special dose adjustment is required. Because of the possible undesirable-effect profile (see section 4.4), it is recommended to monitor the elderly particularly carefully.

Renal impairment:
No dose reduction is required in patients with mild to moderate impairment to renal function (patients with severe renal insufficiency, see section 4.3).

Hepatic impairment (see section 5.2):
No dose reduction is required in patients with mild to moderate impairment to hepatic function (patients with severe hepatic dysfunction, see section 4.3).

Method of administration
For oral administration and short-term use only.
The film-coated tablets should be swallowed whole with water.
It is recommended that patients with sensitive stomachs take Ibuprofen Lysine 342 mg film-coated tablets with food.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema, or urticaria) in response to aspirin (acetylsalicylic acid) or other non-steroidal anti-inflammatory drugs (NSAIDs).

Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

Severe heart failure (NYHA Class IV), renal failure or hepatic failure (see section 4.4).

Patients with cerebrovascular or other active bleeding.

Patients with unclarified blood-formation disturbances.

Patients with severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake).

Adolescents under 40 kg body weight and children under 12 years of age.

Last trimester of pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

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

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

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

Other NSAIDs:
The use of Ibuprofen with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

SLE and mixed connective tissue disease:
Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (See section 4.8).

Renal:
Renal impairment as renal function may further deteriorate (see sections 4.3 and 4.8).

Hepatic:
Hepatic dysfunction (see sections 4.3 and 4.8).

Cardiovascular and cerebrovascular effects:
Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure as fluid retention, hypertension 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. ≤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.

Gastrointestinal:

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

GI bleeding, ulceration or perforation, which can be fatal has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of GI events.

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

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

Patients with a history of GI 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 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 (see section 4.5).

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

Dermatological:
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 (see section 4.8). Patients appear to be at highest risk for 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. Ibuprofen should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

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 may be advisable to avoid use of Ibuprofen Lysine 342 mg film-coated tablets in case of varicella.

Other notes:

Caution is required in patients:

- with congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria);
- immediately after major surgery;
- who have had hypersensitivity or allergic reactions to other substances, as they could be at an increased risk of hypersensitivity reactions with Ibuprofen Lysine 342 mg film-coated tablets;
- 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 Lysine 342 mg film-coated tablets, therapy must be stopped. Medically required measures, in line with the symptoms, must be initiated by competent persons.

Ibuprofen, the active substance of Ibuprofen Lysine 342 mg film-coated tablets may temporarily inhibit the blood-platelet function (thrombocyte aggregation). Therefore, it is recommended to monitor patients with coagulation disturbances carefully.

In prolonged administration of Ibuprofen Lysine 342 mg film-coated tablets regular control of liver function tests, the kidney function, as well as of the blood count is required.

Prolonged use of any type of painkiller for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained and treatment should be discontinued. The diagnosis of medication overuse headache (MOH) should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of headache medications.

In general, habitual intake of painkillers, particularly a combination of several analgesic substances, 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.

Concomitant use of NSAIDs and alcohol may increase the occurrence of undesirable effects associated with the medicinal product, particularly those that concern the gastrointestinal tract or the central nervous system.

NSAIDs may mask symptoms of infection and fever.

Paediatric population
There is a risk of renal impairment in dehydrated adolescents.

4.5 Interaction with other medicinal products and other forms of interaction

Aspirin (*Acetylsalicylic acid)*: Concomitant administration of ibuprofen and aspirin (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 aspirin (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).

Other NSAIDs including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects (see section 4.4).

Corticosteroids: as these may increase the risk of gastrointestinal ulceration or bleeding (see Section 4.4).

Diuretics, ACE inhibitors, beta-receptor-blockers and angiotensin-II antagonists: NSAIDs may reduce the effect of diuretics and other antihypertensive medicinal products. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor, beta-receptor-blocker or angiotensin-II antagonist and active substances that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter. The concomitant administration of Ibuprofen Lysine 342 mg film-coated tablets and potassium-sparing diuretics may lead to hyperkalaemia.

Anticoagulants. NSAIDs may enhance the effects of anti-coagulants, such as warfarin (See section 4.4).

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see section 4.4).

Digoxin, phenytoin, lithium: The concomitant use of Ibuprofen Lysine 342 mg film-coated tablets with digoxin, phenytoin or lithium preparations may increase serum levels of these drugs. A check of serum-lithium, serum-digoxin and serum-phenytoin levels is not as a rule required on correct use (maximum over 3 days).

Methotrexate: The administration of Ibuprofen Lysine 342 mg film-coated tablets within 24 hours before or after administration of methotrexate may

lead to elevated concentrations of methotrexate and an increase in its toxic effect.

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

Sulphonylureas: Clinical investigations have shown interactions between NSAIDs and antidiabetics (sulphonylureas). Rare cases of hypoglycemia were reported in patients with concomitant use of sulfonylurea and ibuprofen. A check of blood-glucose values is recommended as a precaution on concomitant intake.

Ciclosporin: Increased risk of nephrotoxicity.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

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 haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

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.

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

No specific studies have been conducted with ibuprofen lysine.

Pregnancy:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy

and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for 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, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryofoetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

During the first and second trimester of pregnancy, Ibuprofen Lysine should not be given unless clearly necessary. If Ibuprofen Lysine is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

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

- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with

  oligohydroamniosis; the mother and the neonate, at the end of the

  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 Lysine is contraindicated during the third trimester of pregnancy.

Breast-feeding:

In limited studies ibuprofen and its metabolites appear in breast milk in very low concentrations. Since no harmful effects to infants are known to date, it is usually not necessary to interrupt breast- feeding during short-term use of Ibuprofen Lysine at the recommended doses.

Fertility:

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 as central nervous undesirable effects such as tiredness and dizziness may occur on use of Ibuprofen Lysine 342 mg film-coated tablets at higher dosage, the ability to react and the ability to take part actively in road traffic and to operate machines may be impaired in isolated cases. This applies to a greater extent in combination with alcohol.

4.8 Undesirable effects

The list of the following undesirable effects comprises all undesirable effects that have become known under treatment with ibuprofen, also those under high-dose long-term therapy in rheumatism patients. The stated frequencies, which extend beyond very rare reports, refer to the short-term use of daily doses up to a maximum of 1200 mg ibuprofen for oral dosage forms and a maximum of
1800 mg for suppositories.

It should be taken into account that the following undesirable effects are predominantly dose- dependent and vary inter-individually.

The most commonly observed undesirable effects are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following administration. Less frequently, gastritis has been observed. In particular the risk of gastrointestinal bleeding is dependent on the dose range and the duration of treatment.

Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

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).

Please note that within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Very common (1/10)
Common (1/100 to <1/10)
Uncommon (1/1,000 to <1/100)
Rare (1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

Infections and infestations	Very rare	Exacerbation of infection-related development of necrotising fasciitis) coinciding with the use of non-steroidal anti-inflammatory drugs has been described. This is possibly associated with the mechanism of action of the non-steroidal anti- inflammatory drugs. If signs of an infection occur or get worse during use of Ibuprofen Lysine 342 mg film-coated tablets, the patient is recommended to go to a doctor without delay. It is to be investigated whether there is an indication for an anti-infective/antibiotic therapy.
Blood and lymphatic system disorders	Very rare	Haematopoietic disorders (anaemia, leukopenia, thrombocytopenia, pancytopenia, agranulocytosis). The first signs may be fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe fatigue, nasal and skin bleeding. In these cases, the patient should be advised to discontinue this medicinal product, to avoid any self- medication with analgesics or antipyretics and to consult a physician. The blood count should be checked regularly in long- term therapy.
Immune system disorders	Uncommon	Hypersensitivity reactions with skin rashes and itching, as well as asthma attacks (possibly with drop in blood pressure), aggravated asthma, bronchospasm, dyspnoea. The patient is to be instructed to inform a doctor at once and no longer to take Ibuprofen Lysine 342 mg film- coated tablets in this case.

	Very rare	Severe general hypersensitivity reactions. They may present as face oedema, swelling of the tongue, swelling of the internal larynx with constriction of the airways, respiratory distress, tachycardia, drop in blood pressure up to life-threatening shock. If any of these symptoms occurs, which can happen even upon first use, immediate medical assistance is required. The symptoms of aseptic meningitis with neck stiffness, headache, nausea, vomiting, fever or consciousness clouding have been observed under ibuprofen. Patients with autoimmune disorders (SLE, mixed connective- tissue disease) appear to be predisposed.
Psychiatric disorders	Very rare	Psychotic reactions, depression.
Nervous system disorders	Uncommon	Central nervous system disturbances such as headache, dizziness, sleeplessness, agitation, irritability or tiredness.
Eye disorders	Uncommon	Visual disturbances.
Ear and labyrinth disorders	Rare	Tinnitus.
Cardiac disorders	Very rare	Palpitations, heart failure, myocardial infarction.
Vascular disorders	Very rare	Arterial hypertension, vasculitis.
Gastrointestinal disorders	Common	Gastro-intestinal complaints such as pyrosis, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation and slight gastro-intestinal blood losses that may cause anaemia in exceptional cases.
	Uncommon	Gastrointestinal ulcers, 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. The patient is to be instructed to discontinue the medicinal product and to consult a doctor immediately if severe pain in the upper abdomen or melaena or haematemesis occurs.

Hepatobiliary disorders	Very rare	Hepatic dysfunction, hepatic damage, particularly in long-term therapy, hepatic failure, acute hepatitis.
Skin and subcutaneous tissue disorders	Uncommon	Various skin rashes.
	Very rare	Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis, alopecia. In exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection (see also "Infections and infestations").
Renal and urinary disorders	Rare	Kidney-tissue damage (papillary necrosis) and elevated uric acid concentrations in the blood may also occur rarely.
	Very rare	Formation of oedemas, particularly in patients with arterial hypertension or renal insufficiency, nephrotic syndrome, interstitial nephritis that may be accompanied by acute renal insufficiency. Renal function should therefore be checked regularly.

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 <to be completed nationally>.

4.9 Overdose

Symptoms are unlikely at doses below 100 mg/kg.

Symptoms

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

Management

A specific antidote does not exist. Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of

cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and anti-rheumatic products, non-steroids; propionic acid derivative, ATC Code: M01AE01.
Ibuprofen lysine is the lysine salt of ibuprofen.

Mechanism of action
Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) that in the conventional animal- experiment inflammation models has proven to be effective via prostaglandin-synthesis inhibition. In humans, ibuprofen reduces inflammatory-related pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits ADP- and collagen-induced platelet aggregation.

Following oral administration, ibuprofen lysine dissociates to ibuprofen acid and lysine. Lysine has no recognized pharmacological activity. The pharmacological properties of ibuprofen lysine, therefore, are the same as those of ibuprofen acid.

Clinical efficacy and safety
Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose aspirin (acetylsalicylic acid) on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when a single dose of ibuprofen 400 mg was taken within 8 h before or within 30 min after immediate release aspirin (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 relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5).

5.2 Pharmacokinetic properties

Most pharmacokinetic data obtained following the administration of ibuprofen acid also apply to ibuprofen lysine.

Absorption
On oral application, ibuprofen is partly absorbed in the stomach and then completely in the small intestine.
Peak plasma concentrations occur 1-2 hours after administration of ibuprofen

acid in solid oral immediate-release formulation. However, ibuprofen is more rapidly absorbed from the gastrointestinal tract following the administration of Ibuprofen Lysine 342 mg film-coated tablets with peak plasma concentrations occurring 40 minutes (median T_{max}) after administration in the fasting state.

Distribution
Plasma-protein binding about 99%.

Biotransformation
Ibuprofen is metabolised in the liver (hydroxylation, carboxylation).

Elimination
The elimination half-life in healthy individuals and those with liver and kidney diseases is 1.8 - 3.5 hours. The pharmacologically inactive metabolites are completely eliminated, mainly renally (90%), but also with the bile.

5.3 Preclinical safety data

The subchronic 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. Following administration of maternotoxic doses, an increased incidence of malformations (ventricular septal defects) occurred in the progeny of rats.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose, povidone, sodium starch glycollate type A, colloidal silicon dioxide, magnesium stearate, purified water, isopropyl alcohol, Opadry II White 85F18422 (contains polyvinyl alcohol-partially hydrolyzed, titanium dioxide, poly ethylene glycol and talc) and Opacode Black S-1-17823 (shellac, iron oxide black, N-butyl alcohol, propylene glycol and ammonium hydroxide).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Blister pack: 2 years

Bottle pack:
10 tablets: 2 years (unopened), 4 days (after first opening)

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

A blister pack consisting of opaque, white polyvinyl chloride (PVC)/ polyvinylidene chloride (PVdC) laminate heat sealed to aluminium foil. The blisters are packed in cardboard cartons.

Pack size: 8, 12 and 16 tablets

Or

A bottle pack consisting of high density polyethylene bottle with child resistant closure with wad having induction sealing liner. Outer shell embossed with Push down- CR logo. The bottle is packed in cardboard cartons.

Pack size: 10 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Strides Arcolab International Limited
Unit 4, Metro Centre, Tolpits Lane
Watford, Hertfordshire,
WD18 9SS, United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 28176/0177

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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