SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen Dermogen 400 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 400 mg ibuprofen.

Excipients with known effect:

Each film-coated tablet contains 28.5 mg lactose (as monohydrate)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

White, oblong, biconvex film-coated tablets scored on both sides (length: 17 mm, width: 8 mm).

The score line is not intended for breaking the tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Symptomatic treatment of mild to moderate pain and/or fever

- 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.

Pain and/or fever

Adults and adolescents from 12 years of age (≥ 40 kg body weight):

Initial dose 400 mg ibuprofen. If necessary, additional doses of 400 mg ibuprofen can be taken. The respective dosing interval should be chosen in line with the observed symptoms and the maximum recommended daily dose. It should not be below 6 hours. A total dose of 1200 mg ibuprofen should not be exceeded in any 24-hour period.

Rheumatic diseases

Adults

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

Age	**Single dose**	**Maximum daily dose**
Adults	400 - 800 mg ibuprofen (1 – 2 tablets)	1200 - 2400 mg ibuprofen (3 – 6 tablets)

Adolescents from 15 to 17 years of age

The recommended dose should be adjusted by weight: 20-40 mg/kg daily (max 2400 mg daily) in 3-4 divided doses.

Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

The treating physician decides on the duration of treatment.

In rheumatic diseases the use of Ibuprofen Dermogen can be required for a longer period.

Special populations

Elderly:

No special dose adjustments are required. Due to possible undesirable-effect profile (see section 4.4), it is recommended to monitor the elderly particularly carefully.

Renal insufficiency:

No dose adjustment is required in patients with mild to moderate impairment to renal function

(patients with severe renal insufficiency see section 4.3).

Hepatic insufficiency (see section 5.2):

No dose adjustment is required in patients with mild to moderate impairment to hepatic function (patients with severe hepatic dysfunction see section 4.3).

Paediatric population:

Ibuprofen Dermogen 400 mg film-coated tablets is contraindicated in children younger than 12 years of age and in adolescents below 40 kg body weight.

Method of administration

Oral use.

The tablets should be swallowed whole with a glass of water.

It is recommended that patients with a sensitive stomach take Ibuprofen Dermogen with food.

4.3 Contraindications

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

- Patients with a history of hypersensitivity reactions (e.g. bronchospasm, asthma, rhinitis, angioedema or urticaria) associated with the use of acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs).

- Patients with severe heart failure (NYHA Class IV).

- Patients with severe liver failure or severe renal failure.

- Patients with unclarified blood-formation disturbances.

- Patients with cerebrovascular or other active bleeding.

- History of gastrointestinal bleeding or perforation associated with previous NSAIDs therapy.

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

- Patients with severe dehydration (caused by vomiting, diarrhea or insufficient fluid intake)

- Last three months of pregnancy.

- Children younger than 12 years of age and adolescents

4.4 Special warnings and precautions for use

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

Caution is required in patients with certain conditions, which may be made worse:

- systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8)
- congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria)
- hypertension and/or cardiac impairment as renal function may deteriorate (see sections 4.3 and 4.8)
- renal impairment (see sections 4.3 and 4.8)
- hepatic dysfunction (see sections 4.3 and 4.8)
- directly after major surgery
- in patients who react allergically to other substances, as an increased risk of hypersensitivity reactions occurring also exists for them on use of Ibuprofen Dermogen
- in patients who suffer from hay fever, nasal polyps or chronic obstructive respiratory disorders as an increased risk exists for them of allergic reactions occurring. These may present as asthma attacks (so-called analgesic asthma), Quincke's oedema or urticaria.

Gastrointestinal (GI) safety

The use with concomitant NSAIDs, including cyclo-oxygenase-2 specific inhibitors, increases risk of adverse reactions (see section 4.5) and should be avoided.

Elderly:

The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal (GI) bleeding and perforation which may be fatal (see section 4.2).

Gastrointestinal bleeding, ulceration and perforation:

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events. When GI bleeding or ulceration occurs in patients receiving ibuprofen, it is advised to withdraw the treatment.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses and 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 medicinal products (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 section 4.5).

Patients with a history of GI toxicity, particularly the elderly, are advised to report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medicinal products which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet medicinal products such as acetylsalicylic acid (see section 4.5).

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).

NSAIDs may mask symptoms of infection and fever.

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 (see section 4.8). 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. Patients should be advised to discontinue the intake of Ibuprofen Dermogen 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 is advisable to avoid use of Ibuprofen Dermogen in case of varicella.

Cardiovascular and cerebrovascular effects:

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive 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. ≤ 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.

Other notes

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

Ibuprofen 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 Dermogen regular checking of the liver values, 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 terms, the habitual intake of painkillers, particularly on combination of several pain-relieving active 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. Therefore it should be avoided.

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.

The risk of renal failure is increased in dehydrated patients, the elderly and those taking diuretics and ACE inhibitors

Masking of symptoms of underlying infections

Ibuprofen Dermogen 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 Dermogen is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

Patients who report eye disorders during treatment with Ibuprofen should discontinue therapy and be submitted to eye examinations.

Renal tubular acidosis and hypokalaemia may occur following acute overdose and in patients taking ibuprofen products over long periods at high doses (typically greater than 4 weeks), including doses exceeding the recommended daily dose.

Ibuprofen Dermogen contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Lithium: NSAIDs may reduce lithium renal clearance, which will result in an increase of plasma levels and toxicity. If ibuprofen is prescribed to a patient receiving lithium therapy, a close monitoring on the levels of lithium should be conducted.

Methotrexate: NSAIDs may inhibit the tubular secretion of methotrexate and reduce its clearance. The administration of Ibuprofen Dermogen within 24 hours before or after administration of methotrexate may lead to elevated concentrations of methotrexate and an increase in its toxic effect.

Digoxin: The concomitant use of Ibuprofen Dermogen with digoxin may increase serum levels of digoxin. A check of serum-digoxin is recommended.

Phenytoin: The concomitant use of Ibuprofen Dermogen with phenytoin may increase serum levels of these medicinal products. A check of serum-phenytoin levels is recommended.

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

Ciclosporin: The risk of a kidney-damaging effect due to ciclosporin is increased through the concomitant administration of certain nonsteroidal anti-inflammatory drugs. This effect also cannot be ruled out for a combination of ciclosporin with ibuprofen.

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

Diuretics, Angiotensin Converting Enzyme Inhibitors (ACE), betareceptor-blockers and Angiotensin II Antagonists (AIIA): nonsteroidal anti-inflammatory drugs may reduce the efficacy of diuretics, as well as of other anti-hypertensive, betareceptor-blockers and diuretic medicinal products. Diuretics may also increase the NSAIDs nephrotoxicity risk. In some patients with a decreased renal function (dehydrated patients or elderly with compromised renal function), the co-administration of an ACE, betareceptor-blockers or of an angiotensin II antagonist (AIIA) and inhibitors of cyclooxygenase 2 may progress to a deterioration of the renal function, including the possibility of acute renal failure, which is normally 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.

Potassium sparing diuretics: The concomitant administration of Ibuprofen Dermogen and potassium-sparing diuretics may lead to hyperkalaemia (check of serum potassium is recommended).

Other NSAIDs, including salicylates: The concomitant administration of several NSAIDs may increase the risk of gastrointestinal ulcers and bleeding due to a synergistic effect. The 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 addictive effect (see section 4.4).

Corticosteroids: increase on the risk of ulceration or gastrointestinal bleeding (see section 4.4).

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

Anti-platelet medicinal products and selective serotonin reuptake inhibitors: increase on the risk of gastrointestinal bleeding (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).

Aminoglycosides: NSAIDs may reduce the elimination of aminoglycosides.

Ginkgo Biloba: it may boost the risk of bleeding.

Quinolone antibiotics: animal data report that NSAIDs, in combination with quinolone antibiotics, may increase the risk of convulsions. Patients taking NSAIDs and quinolones may present an increased risk of developing convulsions.

Sulfonylureas: NSAIDs may increase the effects of sulfonylureas. Rare cases of hypoglycemia were reported in patients with concomitant administration of sulfonylurea and ibuprofen. A check of blood-glucose values is recommended as a precaution on concomitant intake.

Tacrolimus: possible increased risk of nephrotoxicity when a NSAID is administered with tacrolimus.

Zidovudine: increased risk of hematological toxicity when a NSAID is administered with zidovudine. There is an evidence of an increased risk of hemarthrosis and hematoma in HIV (+) hemophilic patients receiving concomitant treatment with zidovudine and other NSAIDs.

CYP2C9 inhibitors: the concomitant administration of ibuprofen with CYP2C9 inhibitors may increase the exposure to ibuprofen (CYP2C9 substrate). In a study with voriconazol and fluconazol (CYP2C9 inhibitors), it was demonstrated a higher exposure of S (+)-ibuprofen of around 80 to 100%. A dose reduction of ibuprofen should be considered when CYP2C9 inhibitors are concomitantly administered, especially when high doses of ibuprofen are administered with voriconazol or fluconazol.

4.6 Fertility, pregnancy and lactation

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 embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.
From the 20th week of pregnancy onward, Ibuprofen Dermogen 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 trimester of pregnancy, Ibuprofen Dermogen should not be given unless clearly necessary. If Ibuprofen Dermogen 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. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to Ibuprofen Dermogen for several days from gestational week 20 onward. Ibuprofen Dermogen should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

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

- the fœtus to:
  - cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
  - renal dysfunction (see above), which may progress to renal failure with oligo-hydroamniosis;
- 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 Dermogen is contraindicated during the third trimester of pregnancy (see section 4.3).

Breast-feeding

Only small amounts of the active substance ibuprofen and its metabolites pass into human milk. Since harmful effects to infants have not become known to date,

interruption of breast-feeding is usually not necessary during short-term treatment with the recommended dose.

Fertility

The use of ibuprofen may impair female 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.

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 extend in combination with alcohol.

4.8 Undesirable effects

With the following adverse drug reactions, it must be accounted for that they are predominantly dose-dependent and vary interindividually.

The most commonly observed adverse reactions 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. Particularly the risk of gastrointestinal bleeding occurring is dependent on the dose range and the duration of use.

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

Clinical studies suggest that use of ibuprofen, particularly at high dose (2400 mg daily) 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.

The following frequency groupings for undesirable effects are used: 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) and Not known (cannot be estimated from the available data).

System organ class	Frequency	Undesirable effects

Infections and infestations	Very rare	Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of nonsteroidal antiinflammatory drugs has been described. This is possibly associated with the mechanism of action of the nonsteroidal antiinflammatory drugs. If signs of an infection occur or get worse during use of Ibuprofen Dermogen, the patient is therefore recommended to go to a doctor without delay. It is to be investigated whether there is an indication for an antiinfective/antibiotic therapy. The symptoms of aseptic meningitis with neck stiffness, headache, nausea, vomiting, fever or clouding of consciousness have been observed under ibuprofen.
Blood and lymphatic system disorders	Very rare	Anaemia Leukopenia Thrombocytopenia Pancytopenia Agranulocytosis Eosinophilia Coagulopathy (changes in coagulation) Aplastic anemia Hemolytic anemia Neutropenia The first signs may be fever, sore throat, superficial wounds in the mouth, influenza-like complaints, severe lassitude, nosebleeds and skin bleeding. 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) The patient is to be instructed to inform a doctor at once and no longer to take Ibuprofen Dermogen 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, racing heart, drop in blood pressure up to life-threatening shock. If one of these symptoms occurs, which can happen even on first use, the immediate assistance of a doctor is required.
Metabolism and nutrition disorders	Very rare	Hypoglycemia Hyponatremia
	Unknown	Hypokalaemia*
Psychiatric disorders	Very rare	Psychotic reactions Hallucinations Confusion Depression Anxiety
Nervous system disorders	Common	Central nervous disturbances such as dizziness, headaches, sleeplessness, agitation, irritability or tiredness
	Unknown	Paraesthesiae Optic neuritis
Eye disorders	Uncommon	Visual disturbances
Ear and labyrinth disorders	Rare	Tinnitus Loss of hearing
Cardiac disorders	Very rare	Palpitations Heart failure Myocardial infarction
Vascular disorders	Very rare	Hypertension Vasculitis
Respiratory, thoracic and mediastinal disorders	Very rare	Asthma Dyspnea

		Bronchospasm
	Unknown	Rhinitis.
Gastrointestinal disorders	Very 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.
	Common	Gastrointestinal ulcers, potentially with bleeding and perforation. Ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4)
	Uncommon	Gastritis
	Very rare	Oesophagitis, pancreatitis, formation of intestinal diaphragm-like strictures. The patient is to be instructed to withdraw the medicinal product and to go to a doctor immediately if relatively 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 Jaundice
Skin and subcutaneous tissue disorders	Very rare	Bullous reactions including Stevens-Johnson Syndrome and toxic epidermal necrolysis (Lyell syndrome) Erythema multiforme Severe skin infections and soft-tissue complications may occur during a varicella infection (see also "Infections and infestations") Alopecia Purpura

	Unknown	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), acute generalised exanthematous pustulosis (AGEP). Photosensitivity reactions
Renal and urinary disorders	Uncommon	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.
	Rare	Kidney-tissue damage (papillary necrosis), elevated uric acid concentrations in the blood, elevated urea concentration in the blood
	Unknown	Impaired renal function Renal tubular acidosis*

*Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting typically following prolonged use of the ibuprofen component at higher than recommended doses.

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 Yellow Card Scheme at Website: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms
Central nervous disturbances such as headache, dizziness, light-headedness and unconsciousness (also myoclonic convulsions in children), as well as abdominal pain, nausea and vomiting, may occur as symptoms of an overdose. In addition, gastrointestinal bleeding, as well of functional disturbances of the liver and kidneys, is possible. There may furthermore be hypotension, respiratory depression and cyanosis. In serious poisoning metabolic acidosis may occur.

Management
A specific antidote does not exist.
Oral administration of activated charcoal should be considered if the patient presents within 1 hour of ingestion of a potentially toxic amount.

Prolonged use at higher than recommended doses may result in severe hypokalaemia and renal tubular acidosis. Symptoms may include reduced level of consciousness and generalised weakness (see section 4.4 and section 4.8).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiinflammatory and antirheumatic products, non-steroids; propionic acid derivatives

ATC code: M01AE01

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 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.

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

On oral application, ibuprofen is partly absorbed in the stomach and then completely in the small intestine.

Following hepatic metabolisation (hydroxylation, carboxylation), the pharmacologically inactive metabolites are completely eliminated, mainly renally (90 %), but also with the bile. The elimination half-life in healthy individuals and those with liver and kidney diseases is 1.8-3.5 hours, plasma-protein binding about 99 %.

Peak plasma levels following oral administration of a normal-release pharmaceutical form (tablet) are reached after 1 - 2 hours.

5.3 Preclinical safety data

In animal trials, the subchronic and chronic toxicity of ibuprofen showed up mainly in form of lesions and ulcerations in the gastrointestinal tract.

In vitro and *in vivo* studies revealed 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 inhibited ovulation in rabbits and impaired implantation in various animal species (rabbit, rat, mouse). Experimental studies in rat and rabbit have shown 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

Tablet core

Hypromellose

Croscarmelose sodium

Lactose monohydrate,

Microcrystalline cellulose

Pregelatinized starch (maize),

Colloidal anhydrous silica

Magnesium stearate.

Film-coating

Hypromellose

Titanium dioxide (E171)

Talc

Propylene glycol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

42 months

6.4 Special precautions for storage

Do not store above 30ºC

6.5 Nature and contents of container

Ibuprofen Dermogen 400 mg film-coated tablet packed in Al-PVC/PVDC blisters in packs of 20, 30 and 60 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Dermogen Farma, S.A.

C/ Aragoneses, 15 Polígono

Ind. Alcobendas

28108 Alcobendas (Madrid),

Spain

8 MARKETING AUTHORISATION NUMBER(S)

PL 37159/0002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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