SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ibuprofen Denk 400

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: ibuprofen
Each film-coated tablet contains 400 mg ibuprofen.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets
Oblong, smooth, white film-coated tablets with break line on both sides. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of pain and inflammation in case of:
- acute arthritis (including gout),
- chronic arthritis, especially rheumatoid arthritis (chronic polyarthritis),
- spondylitis ankylosans (Morbus Bechterew) and other inflammatory ailments of the spine,
- irritations in case of degenerative joint and spinal ailments (arthrosis and spondylarthrosis),
- soft tissue rheumatism,
- painful swelling and inflammation after injury.

Short-term symptomatic treatment of:
- mild to moderate pain, e.g. head and tooth-ache, menstrual pain,
- fever.

4.2 Posology and method of administration

a) <u>For alleviating pain and reducing fever</u>

Adults and adolescents over the age of 15 (≥ 40 kg):
400 mg of ibuprofen is an effective individual dose. The total daily dose should not exceed 1200 mg, corresponding to 3 film-coated tablets per day.

Age	**Single dose:** **Number of Ibuprofen Denk 400 film-coated tablets**	**Total daily dose*:** **Number of Ibuprofen Denk 400 film-coated tablets**
Adults and adolescents over the age of 15 (≥ 40 kg)	**1** (corresponds to 400 mg ibuprofen)	**3** (corresponds to 1200 mg ibuprofen)

*The respective dosing interval depends on the symptoms and the maximum total daily dose. It should not be less than 6 hours.

b) For anti-rheumatic therapy

The dosage of ibuprofen administered depends upon body weight and age.
The recommended dose range for adults and adolescents over the age of 15 is between 1200 mg and 2400 mg of ibuprofen per day. The maximum single dose for **adults** should not exceed 800 mg of ibuprofen.

Age	**Single dose:** **Number of Ibuprofen Denk 400 film-coated tablets**	**Total daily dose*:** **Number of Ibuprofen Denk 400 film-coated tablets**
Adults	**1-2** (corresponds to 400 mg – 800 mg ibuprofen)	**3-6** (corresponds to 1200 mg – 2400 mg ibuprofen)
Adolescents 15 years and older	**1** (corresponds to 400 mg)	

*The respective dosing interval depends on the symptoms and the maximum total daily dose. It should not be less than 6 hours.

The attending doctor will decide how long the treatment should take.
Long-term treatment with ibuprofen may be required for patients with rheumatic disease.

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

Special patient groups

Elderly patients:
No particular dosage adjustment is required. Due to the potential adverse drug reactions (refer to section 4.4), elderly patients should be carefully monitored.

Impaired renal function:
A dose reduction is not necessary in patients with slight to moderate renal impairment. (Patients with severe renal impairment, see section 4.3)..

Impaired liver function (see section 5.2):
A dose reduction is not necessary in patients with slight to moderate liver impairment. (Patients with severe liver impairment see section 4.3).

Type of administration
Ibuprofen Denk 400 is swallowed whole with ample fluids and should not be taken on an empty stomach. Patients with sensitive stomachs are advised to take Ibuprofen Denk 400 with meals.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1;
- previous history of bronchospasm, asthma, rhinitis, urticaria or angioedema related to treatment with acetylsalicylic acid or other non-steroidal anti-inflammatory agents;
- unexplained impaired haemopoiesis;
- active or previous history of recurrent peptic ulcers or haemorrhage (2 or more different episodes of proven ulceration or bleeding);
- previous history of gastrointestinal bleeding or perforation related to treatment with non-steroidal anti-rheumatic/anti-inflammatory drugs (NSAIDs);
- cerebrovascular bleeding or other active haemorrhaging;
- severe liver or renal impairment;
- severe heart failure (NYHA Class IV);
- severe dehydration (caused, for example, by vomiting, diarrhoea or insufficient fluid intake);
- final trimester of pregnancy (see section 4.6);
- in children and adolescents under 15 years of age.

The use of Ibuprofen Denk 400 is not recommended in children under the age of 15 years, because of the high concentration of active ingredient. However, there are suitable dosage strengths and/or pharmaceutical forms available for this age group.

4.4 Special warnings and precautions for use

Adverse drug reactions may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (refer to section 4.2).

Gastrointestinal safety
Concurrent treatment with ibuprofen and other NSAIDs, including selective cyclooxigenase-2 inhibitors, should be avoided.

Elderly patients
The elderly have an increased frequency of adverse drug reactions in response to NSAIDs, particularly gastrointestinal bleeding and perforation which may be fatal (see section 4.2).

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 a previous history of serious gastrointestinal events.

The risk of gastrointestinal 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) as well as in the elderly. These patients should commence treatment on the lowest available dose. For these patients as well as those requiring concomitant therapy with low-dose acetylsalicylic acid (ASA) or other medications that could increase the risk of gastrointestinal disorders (see section 4.5), combination therapy with a protective drug such as misoprostol or a proton pump inhibitor should be considered (see section 4.5).

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

If patients develop any gastrointestinal bleeding or ulceration while taking ibuprofen, the treatment should be discontinued.

Caution should be exercised when giving NSAIDs to patients with a history of gastrointestinal disease, such as ulcerative colitis or Crohn's disease, as these conditions may be exacerbated (see section 4.8).

Cardiovascular and cerebrovascular effects
Adequate medical supervision and guidance of patients with hypertension and/or slight to moderate decompensated heart failure is necessary when taking the patient's medical history, as there have been reports of fluid retention and oedema related to 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). 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.

Skin reactions
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell syndrome) 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, as the reactions occurred during the first month of treatment in the majority of cases. Ibuprofen should be discontinued at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity.

In exceptional cases, severe skin infections and soft tissue complications may occur during a varicella infection (refer to section 4.8). Until now, the participation of NSAIDs in an exacerbation of these infections could not be excluded. The administration of ibuprofen should therefore be avoided during chicken-pox (varicella infection).

Other information:
Ibuprofen should only be used in the following cases after careful consideration of the potential benefits and risks:
- certain congenital disorders of porphyrin metabolism (e.g. acute intermittent porphyria);
- systemic lupus erythematosus (SLE) as well as mixed connective tissue disease (see section 4.8).

Close medical supervision is required in the following cases:
- a history of gastrointestinal disease or chronic inflammatory intestinal disease (ulcerative colitis, Crohn's disease);
- hypertension or heart failure;
- impaired renal function;
- dehydration;
- impaired liver function;
- right after major surgery;
- patients suffering from hay fever, nasal polyps or chronic obstructive airway disease, as they are at increased risk of developing allergic reactions. These may manifest as asthma attacks (so-called analgesic asthma), angioedema or urticaria;

- patients who have had allergic reactions to other substances, as they are also at increased risk of developing hypersensitivity reactions when taking ibuprofen.

Severe acute hypersensitivity reactions, such as anaphylactic shock, have been observed in very rare cases.
Treatment with ibuprofen must be discontinued immediately at the first signs of a hypersensitivity reaction. A clinician must carry out the appropriate symptomatic medical treatment.

Ibuprofen, the active ingredient of Ibuprofen Denk 400, may reversibly inhibit platelet function (thrombocyte aggregation). Patients with coagulation defects should therefore be monitored carefully.

Regular monitoring of liver and renal function as well as blood count is required during long-term treatment with ibuprofen.

Prolonged use of painkillers may cause headaches which must not be treated with increased doses of the medication.

More generally, regular use of painkillers, particularly in combination with other analgesics, may cause permanent kidney damage associated with the risk of renal failure (analgesic nephropathy).

Concurrent use of NSAIDs with alcohol may enhance the adverse drug reactions, particularly those that affect the gastrointestinal tract or central nervous system.

NSAID can mask the symptoms of infection or fever.

Children and adolescents
There is a risk of renal impairment in dehydrated children and adolescents.

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen, like other NSAIDS, should be used with caution in combination with the following medicines:

Other NSAIDs including salicylates:
Concurrent use of several NSAIDs may increase the risk of gastrointestinal ulceration and haemorrhage due to the synergistic effect. The use of ibuprofen with concomitant NSAIDs should therefore be avoided (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).

Digoxin, phenytoin, lithium:
Concomitant use of ibuprofen with digoxin, phenytoin or lithium preparations may increase plasma levels of these drugs. Monitoring of lithium plasma levels is necessary while monitoring of digoxin and phenytoin plasma levels is recommended.

Diuretics, ACE inhibitors, beta receptor blockers and angiotensin-II antagonists:
Non-steroidal antirheumatic agents may diminish the effect of diuretics and antihypertensives. In patients with impaired renal function, such as exsiccated patients or elderly patients with impaired renal function, concurrent use of an ACE inhibitor, beta receptor blocker or angiotensin-II antagonists with a drug that inhibits cyclooxygenase may cause further deterioration of renal function including acute renal failure, which is reversible as a rule. Combination therapy such as this should therefore only be used with caution, particularly in elderly patients. Patients must be requested to take sufficient fluids and regular monitoring of renal function should be considered after commencing combination therapy.
Concurrent treatment with ibuprofen and potassium-sparing diuretics may cause hyperkalaemia.

Glucocorticoids:
Increased risk of gastrointestinal ulceration or haemorrhage (refer to section 4.4).

Anti-platelet agents and selective serotonin-reuptake inhibitors (SSRI):
Increased risk of gastrointestinal haemorrhage (refer to section 4.4).

Methotrexate:
The use of ibuprofen within 24 hours prior to or after the administration of methotrexate may cause increased methotrexate levels as well as an increase in its adverse drug reactions.

Ciclosporin:
There is an increased risk of nephrotoxicity when ciclosporin is administered concomitantly with certain non-steroidal antirheumatic agents. This effect cannot be ruled out for concurrent treatment with ciclosporin and ibuprofen.

Anticoagulants:
Non-steroidal antirheumatic agents may enhance the effect of anticoagulants, such as warfarin (see section 4.4).

Sulfonylureas:
Clinical studies have demonstrated interactions between non-steroidal antirheumatic agents and oral antidiabetics (sulfonylureas). Blood sugars should be monitored as a precautionary measure during concurrent treatment.

Tacrolimus:
There is an increased risk of nephrotoxicity when both medications are given concomitantly.

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

Probenecid and sulfinpyrazone:
Drugs containing probenecid or sulfinpyrazone may delay excretion of ibuprofen.

Quinolone antibiotics
Data from animal experiments indicate that NSAID can increase the risk of seizures associated with quinolone antibiotics. The risk of seizures developing may be increased in patients who are taking NSAID and quinolone simultaneously.

CYP2C9 inhibitors
Concomitant use of ibuprofen and CYP2C9 inhibitors can increase exposure to ibuprofen (a CYP2C9 substrate). A study with voriconazole and fluconazole (CYP2C9 inhibitors) demonstrated an increase of about 80-100% in exposure to S(+)-ibuprofen. A reduction in ibuprofen dose should be considered if potent CYP2C9 inhibitors are used simultaneously, particularly when high doses of ibuprofen are administered together with either voriconazole or fluconazole.

Gingko biloba
Ginkgo biloba can increase the risk of bleeding associated with NSAID.

4.6 Fertility, pregnancy and lactation

Pregnancy
The inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo and foetal development. Data from epidemiological studies indicate an increased risk of miscarriage as well as cardiac defects and gastroschisis with the use of prostaglandin synthesis inhibitors in early pregnancy. The absolute risk of cardiovascular malformations increased from less than 1% to about 1.5%. It is assumed that the risk is higher with increasing doses and longer duration of therapy.

Animal studies have proven that the use of prostaglandin synthesis inhibitors is related to an increase in pre-and post-implantation loss and embryo and foetal lethality. Further, there have been reported increased incidences of various defects, including cardiovascular defects, in animals that received a prostaglandin synthesis inhibitor during the phase of organogenesis.

Ibuprofen should therefore only be given during the first and second trimesters of pregnancy if absolutely necessary. If ibuprofen is being used by a woman who is attempting to conceive or during the first or second trimesters of pregnancy, the dosage should be kept as low as possible and the duration of treatment as short as possible.

During the third trimester of pregnancy all prostaglandin synthesis inhibitors may:
- expose the foetus to the following risks:
    - cardiopulmonary toxicity (with premature closure of the foetal ductus arteriosus and pulmonary hypertension);
    - renal impairment that may progress to renal failure associated with oligohydramnios;

- expose mother and child to the following risks at the end of the pregnancy:
    - potential prolongation of bleeding time, an inhibiting effect on platelet aggregation that may occur even at very low doses;
    - inhibition of uterine contractions resulting in delayed onset and increased duration of labour.

Ibuprofen is therefore contraindicated during the third trimester of pregnancy.

Breast-feeding
The active ingredient ibuprofen and its breakdown products are excreted only in very low concentrations in breast milk. As it is not known to affect breast-fed infants adversely, weaning is not generally necessary for short-term use. However, if prescribed for a longer period of time and/or at higher doses, early weaning should be considered.

Fertility
The use of ibuprofen, like the use of other drugs that are known to inhibit cyclooxygenase/ prostaglandin synthesis, may cause impairment of female fertility and is therefore not recommended for women who are attempting to conceive. Withdrawal of ibuprofen should be considered in women who are having difficulties becoming pregnant or who are undergoing investigation of infertility.

4.7 Effects on ability to drive and use machines

As central nervous system disorders, such as tiredness or dizziness may occur when using ibuprofen at higher doses, reactivity and the ability to drive and operate machinery may be affected in individual cases. This applies in particular in combination with alcohol.

4.8 Undesirable effects

Adverse drug reactions are classified as follows:

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

Please note that the following adverse drug reactions are mostly dose-dependent and may differ between individuals.

The most common adverse drug reactions affect the digestive tract. Peptic ulcers, perforation or bleeding, sometimes fatal, may occur, particularly in elderly patients (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, indigestion, abdominal pain, melena, hematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease have been reported after use. Gastritis is less common. The risk of gastrointestinal haemorrhaging in particular is dependent upon the dose range and duration of treatment.

Oedema, high blood pressure and heart failure have been reported in response to 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).

Infections and parasitic diseases
There have been very rare reports of exacerbation of inflammation caused by infection, e.g. development of necrotic fasciitis, in association with systemic use of non-steroidal anti-inflammatory drugs. This could be related to the mechanism of action of non-steroidal anti-inflammatory agents.

If signs of an infection occur or worsen during treatment with ibuprofen, the patient is therefore advised to consult a doctor without delay. It should be checked whether anti-infective or antibiotic therapy is indicated.

In very rare cases, the use of ibuprofen has been associated with symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or clouding of consciousness. Patients with autoimmune disease, such as SLE or mixed connective tissue disease, seem to be predisposed to this.

Blood and lymphatic system disorders
Very rare: Impaired hemopoiesis (anaemia, leukopenia, thrombocytopenia, pancytopenia, agranulocytosis).
The first signs could be: fever, sore throat, superficial lesions in the mouth, influenza-like complaints, exhaustion, nose bleeding and dermatorrhagia.

In these cases, the patient should be instructed to discontinue Ibuprofen Denk 400 immediately, to avoid any self-treatment with analgesics or antipyretics and to consult the doctor.

The blood count should be monitored regularly during long-term therapy.

Immune system disorders
Uncommon: Hypersensitivity reactions with rash and pruritus as well as asthma attacks (sometimes with drop in blood pressure).
The patient should be advised to contact a doctor in such a case and to stop taking ibuprofen.

Very rare: Severe general hypersensitivity reactions that may manifest as: facial oedema, swelling of the tongue, inner swelling of the larynx with restriction of the respiratory passages, laboured breathing, palpitations, fall in blood pressure and life-threatening shock.

Immediate medical attention is required if any of these symptoms occur, and this is possible following the first application.

Psychiatric disorders:
Very rare: Psychotic reactions, depression.

Nervous system disorders
Common: Central nervous system disorders, such as headache, dizziness, insomnia, excitability, irritability or fatigue.

Eye disorders
Uncommon: Impaired vision. In this case, the patient should be instructed to inform the doctor immediately and to discontinue the use of ibuprofen.

Disorders of the ear and labyrinth
Very rare: Tinnitus.

Heart disease
Very rare: Palpitations, oedema, heart failure, heart attack.

Vascular disorders
Very rare: Arterial hypertension.

Gastrointestinal disorders
Very common: Gastrointestinal complaints, such as heartburn, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation and slight gastrointestinal bleeding that can cause anaemia in exceptional cases.
Common: Gastrointestinal ulceration, sometimes with bleeding and perforation. Ulcerative stomatitis, exacerbation of colitis or Crohn's disease (see section 4.4).
Uncommon: Gastritis
Very rare: Oesophagitis, pancreatitis, development of intestinal, diaphragm-like strictures.
The patient should be instructed to stop taking the medication if he/she experiences upper abdominal pain, melena or haematemesis and to seek medical help immediately.

Hepatobiliary disorders
Very rare: Liver impairment, liver damage, particularly during long-term therapy, liver failure, acute hepatitis.
The liver parameters should be monitored regularly during long-term treatment.

Skin and subcutaneous tissue disorders
Very rare: Bullous skin reactions, such as Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell syndrome), alopecia.
Not known: Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome).

In exceptional cases, severe skin infections and soft tissue complications may occur during a varicella infection (see also "Infections and parasitic diseases").

Renal and urinary disorders
Uncommon: Oedema, particular in patients with arterial hypertension or renal failure; nephrotic syndrome; interstitial nephritis that may be associated with acute renal failure.
Renal tissue damage (papillary necrosis) and hyperuricaemia are very rare.

Renal function should be monitored 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.

4.9 Overdose

a) Symptoms of an overdose
The symptoms can include nausea, stomach pain, vomiting (may be blood streaked), headache, ringing in the ears, confusion, shaky eye movement, weakness, dizziness, drowsiness, loss of consciousness and convulsions (including myoclonic seizures mainly in children). Gastrointestinal bleeding and liver and renal impairment may also occur.
In serious poisoning metabolic acidosis may occur.
Furthermore, hypothermia, hypotension, respiratory depression and cyanosis may occur.

b) Medical treatment in case of overdose
There is no specific antidote.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Non-steroidal anti-inflammatory drug; propionic acid derivatives
ATC code: M01AE01

Ibuprofen is a non-steroidal anti-inflammatory/anti-rheumatic agent that has demonstrated its efficacy by inhibition of prostaglandin synthesis in the usual animal studies on inflammation. In humans ibuprofen reduces inflammatory 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

When taking orally, ibuprofen is absorbed partly in the stomach and then completely in the small intestine. Following hepatic metabolism (hydroxylation, carboxylation), the pharmacologically ineffective metabolites are eliminated completely, primarily via the kidneys (90 %), but also in bile. The elimination half-life is 1.8–3.5 hours in healthy subjects as well as those with liver or renal impairment while plasma protein binding is about 99 %. Maximum plasma levels are reached 1–2 hours after oral ingestion of a normal release pharmaceutical product.

5.3 Preclinical safety data

Subchronic and chronic toxicity of ibuprofen in animal studies manifested predominately as lesions and ulcers in the gastrointestinal tract.
In-vitro and *in-vivo* examinations revealed no clinically relevant evidence of mutagenic effects of ibuprofen. Studies in rats and mice revealed no evidence of carcinogenic effects of ibuprofen. Ibuprofen caused inhibition of ovulation in the rabbit and interfered with implantation in various animal species (rabbit, rat and mouse). Experimental studies in the rat and rabbit have shown that ibuprofen crosses the placental barrier. After administration of maternal toxic doses, there were increased incidences of deformities (ventricular septal defects) among the descendants.

Ibuprofen presents a risk to aquatic life in surface waters (see section 6.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch, potato starch, sodium starch glycolate (type A), pre-gelatinised starch, colloidal anhydrous silica, magnesium stearate, macrogol 6000, hypromellose, talc, titanium dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Store in a dry place below 30°C.

6.5 Nature and contents of container

Blister packs of PVC/PVDC-aluminium.
Pack sizes: 100 or 20 film-coated tablets.

6.6 Special precautions for disposal

This medicinal product presents 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

DENK PHARMA GmbH & Co. KG
Prinzregentenstr. 79
81675 München
Germany

8. MARKETING AUTHORISATION NUMBER IN GERMANY

2129.98.99

9. DATE OF FIRST AUTHORISATION IN GERMANY

21/08/2012

10. DATE OF REVISION OF THE TEXT

05.2019

11. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription