SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Ibuprofen 200 mg/5 ml oral suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
1 ml oral suspension contains 40 mg Ibuprofen.

Excipients: Maltitol liquid 500 mg/ml and 5.32 mg Sodium per 1 ml oral suspension.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Oral suspension

White or off-white viscous suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Ibuprofen Oral Suspension is used as short-term symptomatic treatment of:
• mild to moderate pain such as dental pain, headache.
• fever.

Ibuprofen Oral Suspension is for use in children from 10 kg body weight (1 year of age), adolescents and adults.

4.2 Posology and method of administration
The dosage is in line with the details in the following table. In children and adolescents, Ibuprofen Oral Suspension is dosed depending on body weight (BW), as a rule with 7 to 10 mg/kg BW as a single dose to a maximum of 30 mg/kg BW as the total daily dose.

The respective dosing interval should be chosen in line with the symptomatology and the maximum daily dose. It should not be below 6 hours. The recommended maximum dose should not be exceeded.
If in children this product is required for more than 3 days, or if the symptoms worsen a doctor should be consulted.

If in adolescents and adults this product is required for more than 3 days in case of fever or for more than 4 days for the treatment of pain, or if the symptoms worsen a doctor should be consulted.

The package includes an oral syringe for oral administration of Ibuprofen Oral Suspension. The oral syringe is graduated in 0.25 ml steps up to 5 ml.

5 ml oral suspension corresponds to 200 mg ibuprofen.

The bottle has to be shaken vigorously before use.

Ibuprofen Oral Suspension 200 mg/5ml:

<table>
<thead>
<tr>
<th>Body Weight (Age)</th>
<th>Single dose</th>
<th>Total daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 kg – 15 kg (Infants/Children 1 – 3 years)</td>
<td>100 mg ibuprofen</td>
<td>300 mg ibuprofen</td>
</tr>
<tr>
<td>16 kg - 19 kg (Children 4 – 5 years)</td>
<td>150 mg ibuprofen</td>
<td>450 mg ibuprofen</td>
</tr>
<tr>
<td>20 kg - 29 kg (Children 6 – 9 years)</td>
<td>200 mg ibuprofen</td>
<td>600 mg ibuprofen</td>
</tr>
<tr>
<td>30 kg - 39 kg (Children 10 – 11 years)</td>
<td>200 mg ibuprofen</td>
<td>800 mg ibuprofen</td>
</tr>
<tr>
<td>≥ 40 kg (Adolescents ≥ 12 years and adults)</td>
<td>200 – 400 mg ibuprofen</td>
<td>1200 mg ibuprofen</td>
</tr>
</tbody>
</table>

Special patient groups

Elderly population:
No special dose adjustment is required in the elderly. Because of the possible undesirable effect profile (see section 4.4), the elderly should be monitored 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).

**Paediatric population:**
Ibuprofen Oral Suspension is not recommended for use in children under 1 year of age or under 10 kg body weight

**Method of administration**

For oral administration and short-term use only.
The bottle has to be shaken vigorously before use.
The oral suspension can be taken without regard to meals. People with a sensitive stomach are recommended to take Ibuprofen Oral Suspension during meals.

### 4.3 Contraindications

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

A history of bronchospasm, asthma, rhinitis, angioedema or urticaria associated with the intake of acetylsalicylic acid (ASA) or other non-steroidal anti-inflammatory drugs (NSAIDs).

Unclarified blood-formation disturbances

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.

Cerebrovascular or other active bleeding.

Severe hepatic failure, severe renal failure or severe heart failure.

Severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake).
Pregnant patients, during the last three months of pregnancy.

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 gastrointestinal and cardiovascular risks below).

Gastrointestinal safety

The use of Ibuprofen Oral Suspension with concomitant NSAIDs, including cyclooxygenase-2 selective inhibitors should be avoided.

Elderly:

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

Gastrointestinal bleeding, ulceration and perforation:

Gastrointestinal 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 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), 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 acetylsalicylic acid, or other drugs likely to increase gastrointestinal risk (see below and section 4.5).

Patients with a history of gastrointestinal toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal 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 acetylsalicylic acid (see section 4.5).

When gastrointestinal bleeding or ulceration occurs in patients receiving Ibuprofen Oral Suspension, the treatment should be withdrawn.
NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn’s disease) as these condition may be exacerbated (see section 4.8 – undesirable effects).

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 trial and epidemiological data suggest that use of ibuprofen, particularly at high doses (2400 mg daily) and in long-term treatment 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 daily) is associated with an increased risk of myocardial infarction.

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 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 Oral Suspension should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of a 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 Oral Suspension in case of varicella.

Other information:

Ibuprofen Oral Suspension should only be used after careful consideration of the risk-benefit ratio in:

- congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria),
- systemic lupus erythematosus (SLE) and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8).

Particularly careful medical monitoring is required in the following cases:

- in impaired renal function (as an acute deterioration of the renal function can occur in patients with pre-existing renal disease),
- in dehydration,
• in hepatic dysfunction,
• directly following major surgery,
• in patients with hay fever, nasal polyps, chronic swelling of the nasal mucosa or chronic obstructive respiratory disorders, as they are at greater risk of developing allergic reactions. Such reactions may manifest as asthma attacks (so-called analgesic-induced asthma), Quincke’s oedema or urticaria,
• in patients who react allergically to other substances, as they are likewise at greater risk of developing hypersensitivity reactions during use of Ibuprofen Oral Suspension.

Severe acute hypersensitivity reactions (e.g. anaphylactic shock) have been very rarely observed. Treatment must be discontinued at the first signs of a hypersensitivity reaction following ingestion of Ibuprofen Oral Suspension. Depending on the symptoms, any clinical measures required must be initiated by specialists.

Ibuprofen, the active substance of Ibuprofen Oral Suspension, can temporarily inhibit blood platelet function (blood platelet aggregation). Patients with coagulation disorders should therefore be carefully monitored.

During prolonged administration of Ibuprofen, regular monitoring of liver enzymes, renal function and the blood count is required.

Caution is required in patients already taking other painkilling or fever-lowering medicines or antibiotics.

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.

The habitual use of painkillers, especially that of several painkilling drugs in combination, may quite generally lead to permanent kidney damage with the associated risk of kidney failure (analgesic nephropathy).

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.

NSAIDs may mask symptoms of infection and fever.

This medicinal product contains maltitol liquid. Patients with rare hereditary problems of fructose intolerance should not take this medicine.
This medicinal product contains up to 1.74 mmol (or 39.90 mg) sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen (like other NSAIDs) should only be used with caution together with the following medicinal substances:

Other non-steroidal anti-inflammatory drugs (NSAIDs) and acetylsalicylic acid:

The concomitant administration of two or more NSAIDs can lead to an increased risk of gastrointestinal ulcers and bleeding because of a synergistic effect. Concomitant use of ibuprofen with other NSAIDs must therefore be avoided (see section 4.4).

Low dose acetylsalicylic acid:

Experimental data suggest that ibuprofen may inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional use (see section 5.1).

Digoxin, phenytoin, lithium:

The concomitant use of Ibuprofen Oral Suspension with digoxin, phenytoin or lithium preparations may increase serum levels of these medicinal products. A check of serum-lithium, serum-digoxin and serum-phenytoin levels is not as a rule required on correct use (maximum over 4 days).

Diuretics, ACE inhibitors, betareceptor blocking medicines and angiotensin-II antagonists:

NSAIDs may reduce the effect of diuretics and other antihypertensive drugs. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitors, betareceptor blocking medicines or angiotensin-II antagonists and agents 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 regular monitoring of renal parameters should be considered following initiation of combination therapy.

The concomitant administration of Ibuprofen Oral Suspension and potassium-sparing diuretics may lead to hyperkalaemia.

Corticosteroids:

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

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

Methotrexate:
The use of Ibuprofen Oral Suspension within 24 hours before or after administration of methotrexate may lead to an increased concentration of methotrexate and an increased toxicity.

Sulphonylureas:
Clinical investigations have shown interactions between non-steroidal anti-inflammatory drugs and antidiabetics (sulphonylureas). Although interactions between ibuprofen and sulphonylureas have not been described to date, a check of blood-glucose values is recommended as a precaution on concomitant intake.

Zidovudine:
The concomitant use of Ibuprofen Oral Suspension may increase the risk of joint effusions and bruising in HIV-positive haemophiliacs.

Ciclosporin:
The risk of nephrotoxic effect caused by ciclosporin is increased by the co-administration of certain NSAIDs. This effect also cannot be ruled out for a combination of ciclosporin with ibuprofen.

Tacrolimus:
The risk of nephrotoxicity is increased when this medicinal product is co-administered with Ibuprofen Oral Suspension.

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

CYP2C9 Inhibitors:
Concomitant administration of ibuprofen with CYP2C9 inhibitors may increase the exposure to ibuprofen (CYP2C9 substrate). In a study with voriconazole and fluconazole (CYP2C9 inhibitors), an increased S(+)-ibuprofen exposure by approximately 80 to 100% has been shown. Reduction of the ibuprofen dose should be considered when potent CYP2C9 inhibitors are administered concomitantly, particularly when high-dose ibuprofen is administered with either voriconazole or fluconazole.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

During the first and second trimester of pregnancy, Ibuprofen Oral Suspension should not be given unless clearly necessary. If Ibuprofen 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 oligohydramniosis;

- 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 Oral Suspension is contraindicated during the third trimester of pregnancy (see section 4.3).

Breast-feeding
Ibuprofen and its metabolites pass only in low concentrations into the breast milk. Since harmful effects to infants have not become known to date, an interruption of breast-feeding is usually not necessary during short-term treatment with ibuprofen at the recommended dose (see section 4.2).

**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 Oral Suspension has minor influence on the ability to drive and use machines. Side effects, such as tiredness and dizziness, can occur when using Ibuprofen Oral Suspension. As a result, the ability to react may be altered in individual cases and the ability to take part actively in road traffic and use machines may be impaired. This particularly applies in interaction with alcohol.

### 4.8 Undesirable effects

The listing of undesirable effects below comprises all side effects reported during treatment with ibuprofen, including those reported during high-dose long-term therapy in rheumatism patients. Reported frequencies beyond very rare reports refer to short-term use of daily doses up to a maximum of 1200mg ibuprofen (30 ml Ibuprofen Oral Suspension, maximum daily dose for adults and adolescents from 12 years of age) for oral formulations and a maximum of 1800 mg for suppositories.

The assessment of side effects is based on the following frequency classification:

<table>
<thead>
<tr>
<th>Frequency Classification</th>
<th>Frequency Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common:</td>
<td>( \geq 1/10 )</td>
</tr>
<tr>
<td>Common:</td>
<td>( \geq 1/100 \text{ to } &lt; 1/10 )</td>
</tr>
<tr>
<td>Uncommon:</td>
<td>( \geq 1/1,000 \text{ to } &lt; 1/100 )</td>
</tr>
<tr>
<td>Rare:</td>
<td>( \geq 1/10,000 \text{ to } &lt; 1/1,000 )</td>
</tr>
<tr>
<td>Very rare:</td>
<td>(&lt; 1/10,000 )</td>
</tr>
<tr>
<td>Not known:</td>
<td>(cannot be estimated from the available data)</td>
</tr>
</tbody>
</table>

With the following adverse drug reactions, it must be accounted for that they are predominantly dose-dependent and vary inter-individually.
The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly may occur (see section 4.4). Nausea, vomiting, 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.

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

Clinical trial and epidemiological data suggest that use of ibuprofen (particularly at high doses 2400 mg daily) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

**Infections and infestations**

*Very rare:*

- Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) has been described in temporal association with the systemic use of non-steroidal anti-inflammatory drugs. This is possibly associated with the mechanism of action of the non-steroidal anti-inflammatory drugs.

If signs of an infection occur or get worse during use of Ibuprofen Oral Suspension, the patient is therefore recommended to consult a doctor immediately. It should be ascertained whether there is an indication for an anti-infective/antibiotic therapy.

**Blood and lymphatic system disorders**

*Very rare:*

- Problems with blood formation (anaemia, leukopenia, thrombocytopenia, pancytopenia, agranulocytosis).

Early signs may include: fever, sore throat, superficial wounds in the mouth, flu-like symptoms, pronounced fatigue, nosebleeds and skin bleeding. In such cases, the patient should be advised to discontinue the medicine immediately, 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).

The patient is to be instructed to inform a doctor at once and no longer to take Ibuprofen Oral Suspension in this case.
Very rare: - Signs of aseptic meningitis such as headache, nausea, vomiting, fever, stiff neck or clouding of consciousness. Patients with certain immune system disorders (systemic lupus erythematosus or mixed connective tissue disease) appear to be at increased risk.

- Severe general hypersensitivity reactions. Signs may include: swelling of the face, tongue and internal larynx with airway narrowing, breathlessness, fast heartbeat, blood pressure drop to the point of life-threatening shock.

If one of these symptoms occurs, which can happen even on first use, immediate medical assistance is required.

**Psychiatric disorders**

*Very rare:* - Psychotic reactions, depression.

**Nervous system disorders**

*Uncommon:* - Central nervous disturbances such as headache, dizziness, sleeplessness, agitation, irritability or tiredness.

**Eye disorders**

*Uncommon:* - Visual disturbances. In this case, the patient should be instructed to inform the doctor and to discontinue ibuprofen.

**Ear and labyrinth disorders**

*Rare:* - Tinnitus.

**Cardiac disorders**

*Very rare:* - Palpitations, heart failure, myocardial infarction.

**Vascular disorders**

*Very rare:* - Arterial hypertension

**Gastrointestinal disorders**

*Common:* - Gastro-intestinal symptoms such as heartburn, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation and minor gastro-intestinal blood losses that may cause anaemia in exceptional cases.

*Uncommon:* - Stomach or intestinal ulcers, sometimes 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 use of Ibuprofen Oral Suspension has to be stopped if the patient experiences significant pain in the upper belly, vomits blood, has blood in the stool or black stool.

**Hepatobiliary disorders**

*Very rare:* Hepatic dysfunction, hepatic damage, especially during long-term treatment, 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 (Lyell’s syndrome), 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:* Renal tissue damage (papillary necrosis), particularly in long-term therapy, increased uric acid concentration in the blood.

*Very rare:* Reduced urinary output and formation of oedemas, particularly in patients with arterial hypertension or renal insufficiency, nephrotic syndrome, interstitial nephritis, that may be accompanied by acute renal insufficiency.

The use of Ibuprofen Oral Suspension has to be stopped if these symptoms occur or get worse.

**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 (www.mhra.gov.uk/yellowcard).

### 4.9 Overdose

**Symptoms of an overdose**

Central nervous disturbances such as headache, dizziness, light-headedness, loss of consciousness (in children also myoclonic seizures), as well as abdominal pain, nausea and vomiting may occur. Moreover, gastrointestinal bleeding, renal dysfunction and hepatic dysfunction are possible Furthermore hypotension, respiratory depression and cyanosis may occur.
Therapeutic measures in overdose

There is no specific antidote to ibuprofen.
The therapeutic options for treatment of intoxication depend on the extent, stage and clinical symptoms according to standard practice in the ICU.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Anti-inflammatory and anti-rheumatic products, non-steroids; Propionic acid derivatives
ATC code: M01AE01

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

Experimental data suggest that ibuprofen may inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 hours before or within 30 minutes after immediate release acetylsalicylic acid dosing (81mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

5.2 Pharmacokinetic properties
On oral application, ibuprofen is already 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 is about 99 %. Peak plasma levels following oral administration of a normal release pharmaceutical form are reached after 1 - 2 hours.
5.3 Preclinical safety data
The subchronic and chronic toxicity of ibuprofen in animal experiments showed up mainly in form of 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 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.

The active substance ibuprofen shows an environmental risk for fish.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Sodium benzoate (E211),
Citric acid anhydrous,
Sodium citrate,
Saccharin sodium,
Sodium chloride,
Hyromellose,
Xanthan gum,
Maltitol liquid,
Glycerol (E422),
Thaumatin (E957),
Strawberry flavour (natural flavouring preparations, maize maltodextrin, triethyl citrate (E-1505), propylene glycol (E-1520) and benzyl alcohol),
Purified water.

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years
After first opening: 6 months
6.4 **Special precautions for storage**
This medicinal product does not require any special storage conditions.

6.5 **Nature and contents of container**
Amber coloured polyethylene terephthalate (PET) bottles of 30 ml, 100 ml, 150 ml and 200 ml with a child-resistant closure, fitted with a low density polyethylene stopper.

The product is supplied with a 5 ml oral syringe, comprising of a high-density polyethylene piston and a polypropylene barrel.

The oral syringe is graduated in 0.25 ml steps up to 5 ml.

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.

No special requirements

7 **MARKETING AUTHORISATION HOLDER**
Aspire Pharma Ltd
Unit 4 Rotherbrook Court
Bedford Road
Petersfield
Hampshire
GU32 3QG
United Kingdom

8 **MARKETING AUTHORISATION NUMBER(S)**
PL35533/0034
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10/12/2014

10 DATE OF REVISION OF THE TEXT

16/02/2017