

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Fenopine for Children Six Plus Strawberry 200mg/5ml Oral Suspension

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of suspension contains 200 mg of ibuprofen.

### Excipients with known effect

Liquid Maltitol 4.25 g/5 ml

Sodium Benzoate (E 211) 10 mg/5 ml

Propylene Glycol (E1520) 5.2 mg/5 ml

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Oral Suspension

White/cream suspension.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Fenopine for Children is indicated in children aged 6 to 12 years.

For the short-term symptomatic treatment of mild to moderate pain.

For the short-term symptomatic treatment of fever.

### 4.2 Posology and method of administration

#### Posology

For pain and fever: The daily dosage for children is 20-30mg/kg bodyweight in divided doses. Using the dosing device provided this can be achieved as follows:

Child's age (weight)	Quantity and method of administration	Frequency (in 24 hour period)
6-9 years (20-29 kg)	1 x 200 mg/5 ml (One 5 ml dose)	3 times
10-12 years (30-40 kg)	1 x 300 mg/7.5 ml (5 ml + 2.5 ml)	3 times

Doses should be given approximately every 6 to 8 hours.

For patients with sensitive stomachs it is recommended that Fenopine for Children is taken during a meal.

*Not intended for children under 6 years of age or under 20kg.*

#### Method of administration

For oral use.

For short-term use only

If this medicinal product is required for more than 3 days, or if symptoms worsen a doctor should be consulted.

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

Renal insufficiency: (see section 5.2)

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 insufficiency: (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).

### **4.3 Contraindications**

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

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

History of gastrointestinal bleeding or perforation, related to NSAID's therapy.

Patients with cerebrovascular or other active bleeding.

Patients with unclarified blood-formation disturbances.

Last trimester of pregnancy (see section 4.6).

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

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

Significant dehydration (caused by vomiting, diarrhoea or insufficient fluid intake).

### **4.4 Special warnings and precautions for use**

Undesirable effects may be minimized by using the minimum effective dose for the shortest possible duration necessary to control symptoms (see section 4.2 GI and cardiovascular risks below)

Patients treated with NSAIDs long term should undergo regular medical supervision to monitor for adverse events

#### *Elderly:*

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

#### *Caution is required in patients:*

- with congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria).
- directly after major surgery.
- with hayfever, nasal polyps or chronic obstructive respiratory disorders as there is an increased risk in such patients of allergic reactions occurring. These may present as asthma attacks (so-called analgesic asthma), Quincke's oedema or urticarial. *Other NSAIDs:*The use of Fenopine for Children with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5). *SLE and mixed connective tissue disease:*Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8). *Renal:*Renal impairment as renal function may further deteriorate (see sections 4.3 and 4.8).Administration of NSAIDs such as ibuprofen may cause dose dependent renal toxicity in patients with reduced

renal blood flow or blood volume where renal prostaglandins support the maintenance of renal perfusion. Patients at risk of this reaction include those with impaired renal function, heart failure or liver dysfunction. This is of particular importance in hypertension and/or cardiac impairment as renal function may deteriorate and/or fluid retention occur. Caution is therefore required in the use of ibuprofen in such patients. There is a risk of renal impairment in dehydrated children and adolescents. *Hepatic:* Hepatic dysfunction (see section 4.3 and 4.8). *Cardiovascular and Cerebrovascular effects:* Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure as fluid retention; hypertension and oedema have been reported in association with NSAID therapy. Clinical trials suggest that use of ibuprofen, particularly at high doses (2400mg/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. 1200mg/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. Cases of Kounis syndrome have been reported in patients treated with Fenopine for Children. Kounis syndrome has been defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to myocardial infarction. 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. *Respiratory:* Ibuprofen should be used with caution in patients with bronchial asthma or allergic disease, since such patients may have NSAID – sensitive asthma which has been associated with severe bronchospasm. *Gastrointestinal:* NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section 4.8). GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events. Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment. The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low-dose acetylsalicylic acid, or other medicinal products likely to increase gastrointestinal risk (see below and section 4.5). Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin (see section 4.5). When GI bleeding or ulceration occurs in patients receiving ibuprofen, the treatment should be withdrawn. *Severe cutaneous adverse reactions (SCARs):* Severe cutaneous adverse reactions (SCARs), including exfoliative dermatitis, erythema multiforme, Stevens- Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome), and acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with the use of ibuprofen (see section 4.8). Most of these reactions occurred within the first month. If signs and symptoms suggestive of these reactions appear ibuprofen should be withdrawn immediately and an alternative treatment considered (as appropriate). 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 Fenopine for Children in case of varicella (Chicken pox.) *Masking of symptoms of underlying infections:* Ibuprofen can mask symptoms of infection, which may lead to delayed initiation of appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to varicella. When ibuprofen 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. *Medication overuse headache* 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. *Product specific warnings:* This medicine contains 10 mg benzoate salt in each 5 ml volume. This medicine contains 5.2 mg propylene glycol in each 5 ml volume. This medicine contains 4.25 g liquid maltitol in each 5 ml volume. Patients with rare hereditary problems of fructose intolerance should not take this medicine. Maltitol may have a mild laxative effect. Calorific value 2.3 kcal/g. This medicine contains less than 1 mmol sodium (23mg) per 5 ml, that is to say essentially 'sodium-free'.

#### 4.5 Interaction with other medicinal products and other forms of interaction

Acetylsalicylic acid (Aspirin): Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects (see section 4.4).

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)

*Other NSAIDs:including cyclooxygenase-2 selective inhibitors:* as a results of synergistic effects, avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects (see section 4.4). Co-adminstration of ibuprofen with other NSAIDs should therefore be avoided (see section 4.4)

*Ticlopidine:* NSAIDs should not be combined with ticlopidine due to a risk of an additive effect in the inhibition of the platelet function.

*Methotrexate:* There is a potential for an increase in plasma methotrexate.

**Ibuprofen should be used with caution in combination with:**

*Anticoagulants:* NSAIDs may enhance the effects of anticoagulants, such as warfarin or heparin (see section 4.4). In case of simultaneous treatments, monitoring of the coagulation state is recommended.

*Diuretics, ACE inhibitors, beta-receptor 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 inhibitor, beta-receptor 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 consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

The concomitant administration of ibuprofen and potassium-sparing diuretics may lead to hyperkalaemia.

*Sulphonylureas:*

Clinical investigations have shown interactions between NSAIDs and antidiabetics (sulphonylureas). Although interactions between ibuprofen and sulphonylureas have not beendescribed to date, a check of blood-glucose values is recommended as a precaution on concomitant intake.

*Probenecid and sulfinpyrazone:*

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

*Corticosteroids:* May increase the risk of adverse reactions in the gastrointestinal tract (see section 4.4 Special warnings).

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

*Cardiac glycosides:* NSAIDs may exacerbate cardiac failure, reduce GFR and increased plasma glycoside levels.

*Ciclosporin:* Increased risk of nephrotoxicity.

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

*Lithium, Phenytoin:* There is evidence for potential increase in plasma levels of these active ingredients. Checking the serum lithium levels is necessary and it is recommended to check the serum phenytoin levels.

*Zidovudine:* Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

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

*Ritonavir*: May increase the plasma concentrations of NSAIDs.

*Moclobemide*: Enhances the effect of ibuprofen.

*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 80-100% has been shown. Reduction of ibuprofen dose should be considered when potent CYP2C9 inhibitors are administered concomitantly, particularly when high-dose ibuprofen is administered with either voriconazole or fluconazole.

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

*Aminoglycosides*: NSAIDs can slow down the elimination of aminoglycosides and increase their toxicity.

*Cholestyramine*: Concomitant treatment with cholestyramine and ibuprofen results in prolonged and reduced (25%) absorption of ibuprofen. The medicinal products should be administered with at least one hour interval.

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

*Baclofen*: Elevated baclofen toxicity.

#### **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 use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimesters of pregnancy, ibuprofen should not be given unless clearly necessary. If ibuprofen is used by a woman attempting to conceive, or during the first and second trimesters 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 for several days from gestational week 20 onward. Ibuprofen should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

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

- Cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- Renal dysfunction, which may progress to renal failure with oligo-hydroamniosis (see above);

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

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

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

##### *Lactation*:

In limited studies, ibuprofen appears in the breast milk in very low concentration and is unlikely to affect breast-fed infants adversely. If, however, longer treatment is prescribed, early weaning should be considered.

##### *Fertility*:

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

#### 4.7 Effects on ability to drive and use machines

None expected at recommended dose and duration of therapy

#### 4.8 Undesirable effects

The following frequencies are taken as a basis when evaluating undesirable effects:

Very common:  $\geq 1/10$

Common:  $\geq 1/100$  to  $< 1/10$

Uncommon:  $\geq 1/1,000$  to  $< 1/100$

Rare:  $\geq 1/10,000$  to  $< 1/1,000$

Very rare:  $< 1/10,000$

Not known: cannot be estimated from the available data

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 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.

Particularly the risk of gastrointestinal bleeding occurring is dependent on the dose range and the duration of use.

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

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

The list of the following undesirable effects comprises all undesirable effects that have become known under treatment with ibuprofen, also those under high-dose long-term therapy in rheumatism patients. The stated frequencies, which extend beyond very rare reports, refer to the short-term use of daily doses up to a maximum of 1200 mg ibuprofen for oral dosage forms and a maximum of 1800 mg for suppositories (= 60 ml oral suspension of Fenopine for Children maximum daily dose for adults and children older than 12 years).

##### Infections and infestations:

Very rare: exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of non-steroidal anti-inflammatory drugs has been described. This is possibly associated with the mechanism of action of the non-steroidal anti-inflammatory drugs.

If signs of an infection occur or get worse during use of this product, the patient is therefore recommended to go to a doctor without delay. It is to be investigated whether there is an indication for an anti-infective/antibiotic therapy.

Very rare: the symptoms of aseptic meningitis with neck stiffness, headache, nausea, vomiting, fever or consciousnesses clouding have been observed under ibuprofen. Patients with autoimmune disorders (SLE, mixed connective-tissue disease) appear to be predisposed.

##### Blood and lymphatic system disorders:

Very rare: Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, and agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising. 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 rash and pruritis, 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 in this case.

Very rare: Severe general hypersensitivity reactions.

They may present as facial 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.

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.

Ear and labyrinth disorders:

Rare: tinnitus.

Cardiac disorders:

Very rare: palpitations, heart failure, myocardial infarction.

Not known: Kounis syndrome.

Vascular disorders:

Very rare: arterial hypertension.

Gastrointestinal disorders:

Common: gastro-intestinal complaints such as pyrosis, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation and slight gastro-intestinal blood losses that may cause anaemia in exceptional cases.

Uncommon: gastrointestinal ulcers, potentially with bleeding and perforation. Ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4), gastritis.

Very rare: oesophagitis, pancreatitis, formation of intestinal, diaphragm-like strictures.

The patient is to be instructed to withdraw the medicinal product and to go to a doctor immediately if severe pain in the upper abdomen or melaena or haematemesis occurs.

Hepatobiliary disorders:

Very rare: Hepatic dysfunction, hepatic damage, particularly in long-term therapy, hepatic failure, acute hepatitis.

Skin and subcutaneous tissue disorders:

Uncommon: Various skin rashes.

Very rare: Alopecia, severe cutaneous adverse reactions (SCARs) (including Erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis).

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

Not Known: Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), acute generalised exanthematous pustulosis (AGEP), Photosensitivity reactions (frequency unknown), fixed drug eruption.

Renal and urinary disorders:

Rare: renal tissue damage (papillary necrosis), particularly in long-term therapy, increased serum uric acid concentration in the blood.

Very rare: reduced urinary excretion 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.

Renal function should therefore be checked regularly.

#### *Investigations*

Rare: increase of blood urea nitrogen, serum transaminases and alkaline phosphatase, decrease in haemoglobin and haematocrit values, inhibition of platelet aggregation, prolonged bleeding time, decrease of serum calcium, increase in serum uric acid

#### **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 HPRA Pharmacovigilance, Website: [www.hpra.ie](http://www.hpra.ie)

#### **4.9 Overdose**

In children ingestion of more than 400 mg/kg may cause symptoms. In adults the dose response effect is less clear cut. The half-life in overdose is 1.5 – 3 hours.

#### **Symptoms**

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

#### **Management**

Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal or gastric emptying if the patient presents within 1 hour of ingestion of a potentially toxic amount. If ibuprofen has already been absorbed, alkaline substances may be administered to promote the excretion of acid ibuprofen in the urine. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma. The local poisons centre should be contacted for medical advice.

## **5 PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

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

ATC Code:M01 AE01

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) that in the conventional animal-experiment inflammation models has demonstrated its efficacy by inhibition of prostaglandin synthesis. 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 (aspirin) on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400 mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5).



## 5.2 Pharmacokinetic properties

### Absorption

On oral application ibuprofen is already partly absorbed in the stomach and then completely in the small intestine, peak serum concentrations occurring 1-2 hours after oral administration of a normal-release pharmaceutical form .

### Distribution

Ibuprofen is rapidly distributed throughout the whole body. The plasma protein binding is approximately 99%.

### Metabolism

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

### Elimination

Ibuprofen is metabolised in the live into two major metabolites with primary excretion via the kidneys. Either as such or as major conjugates, together with negligible amount of unchanged Ibuprofen, excretion by the kidney is both rapid and complete. Elimination half life is approximately 2 hours.

## 5.3 Preclinical safety data

As a well established and widely used product, the pre-clinical safety of ibuprofen is well documented.

The principal findings observed during subchronic and chronic toxicity studies with ibuprofen include gastric damage and ulcers. Any observation made during the in vitro and in vivo studies to investigate the mutagenic potential of ibuprofen were not considered to be clinically significant.

Furthermore no carcinogenic effects have been observed in mice and rats.

Ibuprofen inhibits ovulation in rabbits and impairs implantation in various animal species (rabbit, rat, and mouse). In reprotoxicity studies in rats and rabbits; ibuprofen crossed the placenta. At dose causing toxicity to the mother, malformations (ventricular septal defects) occurred more frequently in the progeny of rats.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Glycerol  
Xanthan gum,  
Liquid Maltitol,  
Polysorbate 80,  
Saccharin sodium,  
Citric acid monohydrate (for pH-adjustment),  
Magnesium Aluminium Silicate,  
Sodium Benzoate (E211),  
Strawberry flavour (contains propylene glycol)  
Purified water

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

36 months  
In use shelf life: 12 months

### 6.4 Special precautions for storage

Do not store above 25°C.

### 6.5 Nature and contents of container

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An amber glass bottle sealed with child resistant, tamper evident cap.

Pack sizes available: 60 ml, 80ml, 100 ml, 150 ml and 200 ml.

Not all pack sizes may be marketed.

A double ended spoon with measures of 1.25ml 2.5ml or 5ml is provided.

#### **6.6 Special precautions for disposal and other handling**

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

#### **7 MARKETING AUTHORISATION HOLDER**

Pinewood Laboratories Ltd

Ballymacarbry

Clonmel

Co. Tipperary

Ireland

#### **8 MARKETING AUTHORISATION NUMBER**

PA0281/088/006

#### **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 18<sup>th</sup> December 2020

#### **10 DATE OF REVISION OF THE TEXT**

May 2024