Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Fenopine 200 mg/5 ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of suspension contains 200 mg of Ibuprofen.

Excipients with known effect	
Liquid Maltitol	4.25g/5ml
Sodium Benzoate (E 211)	10 mg/5ml
Propylene Glycol (E1520)	5.2 mg/5ml

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

Children under 12 years
Ibuprofen 200 mg/5 ml Oral Suspension is indicated for rheumatic or muscular pain, headache, dental pain, feverishness (including post-immunisation pyrexia), symptoms of cold and influenza.

Over 12 years
Ibuprofen 200 mg/5 ml Oral Suspension is indicated for **r**heumatic or muscular pain, pain of non-serious arthritic conditions, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness, symptoms of colds and influenza.

4.2 Posology and method of administration

For oral administration and short-term use only.

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

Leave at least four hours between doses and do not take more than the recommended amount in any 24 hour period.
Not to be given to children under 3 months of age, except on the advice of a doctor
This product should only be given to infants who weigh more than 5kg.

If in children aged from 6 months and in adolescents this medicinal product is required for more than 3 days, or if symptoms worsen a doctor should be consulted. For infants aged 3 - 5 months, medical advice should be sought if symptoms worsen or not later than 24 hours if symptoms persist.

The daily dosage for children is 20- 30mg/kg bodyweight in divided doses. Using the dosing device provided this can be achieved as follows:
3 to 6 months (weighing more than 5 kg): 1.25ml (50mg), up to 3 times in 24 hours.
6 to 12 months (weighing 8-10 kg): 1.25ml (50mg), up to 3 to 4 times in 24 hours.
1 to 4 years (weighing 10-15 kg): 2.5ml (100mg), up to 3 times in 24 hours.
4 to 7 years (weighing 15-20 kg): 3.75ml (150mg), up to 3 times in 24 hours.
7 to 12 years (weighing 20-40 kg): 5 ml (200mg), up to 3 times in 24 hours.

Over 12 years: 5 ml (200mg) to 10ml (400mg) up to three times in 24 hours (maximum daily dose 1200mg)

Post-immunisation pyrexia in infants
1.25ml as a single dose repeated once after 6 hours if necessary.
No more than 2 doses in 24 hours. If fever is not reduced, consult a doctor.

This product is intended for short term use only. Only the lowest dose for the shortest time necessary to relieve symptoms should be used.

Impaired renal function
In patients with mild or moderate reduction of renal function, the dose should be kept as low as possible for the shortest duration necessary to control symptoms and renal function monitored. (For patients with severe renal failure see section 4.3)

Impaired liver function
In patients with mild or moderate reduction of liver function the dose should be kept as low as possible for the shortest duration necessary to control symptoms and hepatic function monitored. (For patients with severe liver failure see section 4,3)

If symptoms persist or worsen consult your doctor.

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.

Last trimester of pregnancy (see section 4.6).

Patients with rare hereditary problems of fructose intolerance should not take this medicine.

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.
Other NSAIDs:
The use of Ibuprofen 200 mg/5 ml Oral Suspension with concomitant NSAIDs including cylooxygenase-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).
Asthmatic patients are to seek their doctor's advice before using ibuprofen (see below)
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 trialssuggest 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.

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 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. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. Ibuprofen 200mg/5ml Oral Suspension should be discontinued at the first appearance of skin rash, mucosal lesion, or any other sign of hypersensitivity.
Exceptionally, varicella can be at the origin of serious cutaneous and soft tissues infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of Ibuprofen Oral Suspension 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 case of varicella, use of ibuprofen should be avoided due to the possible exacerbation of serious cutaneous and soft tissue infectious complications (see "severe skin reactions" above). In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

This medicinal product contains sodium benzoate. Benzoate salt may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old). Increase in bilirubinaemia following its displacement from albumin may increase neonatal jaundice which may develop into kernicterus (non-conjugated bilirubin deposits in the brain tissue).

This medicine product contains Propylene glycol. If your baby is less than 4 weeks old, talk to your doctor or pharmacist before giving them this medicine, in particular if the baby is given other medicines that contain propylene glycol or alcohol. Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce serious adverse effects in neonates.

This medicinal product contains Maltitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

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

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen should be avoided in combination with:
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 Ibruprofen 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 Ibruprofen 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 Fenopine 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 been described 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 Ibruprofen.

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.

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 (pentoxyflline): 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 (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: ≥ 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
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 Ibuprofen Oral Suspension 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.

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, photosentivity
Very rare: Severe forms of skin reactions such as bullous reactions, including Stevens
- Johnson syndrome, erythema multiforme and toxic epidermal necrolysis alopecia.

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

Not Known: Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome). Acute generalised exanthematous pustulosis (AGEP). Photosensitivity reactions (frequency unknown).

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 the national reporting system listed in Appendix V

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 if the patient presents within 1 hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-inflammatory and 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, Fenopine reversibly inhibits ADP – and collagen-inducted 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 Ibruprofen 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 Fenopine is well documented.

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

Furthermore no carcinogenic effects have been observed in mice and rats.
Fenopine inhibits ovulation in rabbits and impairs implantation in various animal species (rabbit, rat, and mouse). In reprotoxicity studies in rats and rabbits; Fenopine 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 25ºC. Store in the original pack.

6.5 Nature and contents of container

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

PA0281/088/005

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st February 2019
Date of last renewal: 31st January 2024

10 DATE OF REVISION OF THE TEXT

July 2023