

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Fenopine 600 mg Film-Coated Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 600 mg of Ibuprofen.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film coated tablet.

Pink, capsule shaped, film-coated tablet with markings 'IBU 600' on one side and plain on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Fenopine tablets are indicated in the management of various arthroses such as rheumatoid arthritis (including juvenile rheumatoid arthritis or Stills disease), osteoarthritis, seronegative arthropathies ankylosing spondylitis and non-articular rheumatic conditions and soft tissue injuries.

Fenopine tablets are also indicated for the treatment of mild to moderate pain.

4.2 Posology and method of administration

For oral administration.

In general, NSAIDs should only be used when an anti-inflammatory effect is required. NSAIDs should be used with particular caution in the elderly who are more prone to adverse events. Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (*see section 4.4, Special warnings and precautions for use*). Treatment should be reviewed at regular intervals and discontinued if no benefit is seen or intolerance occurs.

Adults:

The usual dose is 1200 to 1600mg daily in divided doses. Some patients may be maintained on 600 – 1200 mg daily. The maximum daily dose should not exceed 2400mg.

Elderly:

The recommended adult dose is appropriate. No specific dosage modifications are required unless renal or hepatic function is impaired, in which case dosage should be assessed individually.

Care should be taken in elderly patients in whom increased tissue levels may result from the normal processes of ageing, with an attendant increase in the risk of adverse reactions (which are more likely to be masked by concurrent therapy or disease in the elderly).

Children:

Over 30kg body weight: 20mg/kg daily in divided doses.

20-30kg body weight: The maximum daily dose is 400mg.

Under 20kg body weight: Not recommended.

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

4.3 Contraindications

Fenopine tablets should not be used in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis or urticaria) in response to ibuprofen, aspirin and other non-steroidal anti-inflammatory agents.

History of gastrointestinal bleeding or perforation, related to previous NSAID's therapy. Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

Severe hepatic failure (see section 4.4)

Severe renal failure (see section 4.4)

Severe heart failure (NYHA Class IV) or coronary heart disease (see section 4.4).

4.4 Special warnings and precautions for use

The use of Fenopine tablets with concomitant NSAIDs including cyclooxygenase-2-selective inhibitors should be avoided. Undesirable effects may be reduced by using the minimum effective dose for the shortest possible duration necessary to control symptoms (*see section 4.2, Posology and method of administration and GI and cardiovascular risks below*). Patients treated with NSAIDs long-term should undergo regular medical supervision to monitor for adverse events.

Renal

In patients with renal impairment caution is required as renal function may further deteriorate (see section 4.3 and section 4.8)

Assessment of renal function should occur prior to the initiation of therapy and regularly thereafter. The dose should be kept as low as possible and renal function should be monitored.

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

Use with caution in patients with hepatic dysfunction (see section 4.3 and section 4.8)

Elderly patients are particularly susceptible to the adverse effects of NSAIDs especially gastro-intestinal bleeding and perforation which may be fatal (*see section 4.2, Posology and method of administration*). Prolonged use of NSAIDs in the elderly is not recommended. Where prolonged therapy is required, patients should be reviewed regularly.

Gastrointestinal bleeding, ulceration and perforation

Gastrointestinal bleeding, ulceration or perforation which can be fatal, has been reported with all NSAIDs and can occur at any time during treatment with or without warning symptoms or a previous history of serious gastrointestinal events.

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, Contraindications*) 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 aspirin or other drugs likely to increase gastrointestinal risk (*See section 4.5, Interaction with other medicinal products and other other forms of interactions*).

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 the treatment.

When GI bleeding or ulceration occurs in patients receiving Fenopine Tablets, the treatment should be withdrawn.

NSAIDs should be used with care to patients with a history of gastrointestinal disease (ulcerative colitis or Crohn's disease) as their condition may be exacerbated (*See section 4.8, Undesirable effects*).

Fenopine should also be used with caution in patients with asthma, atopic patients or in patients who have developed bronchospasms with other non-steroidal anti-inflammatory agents.

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, Interaction with other medicinal products and other forms of interactions*).

Signs of intolerance or unwanted effects are indications for stopping treatment.

Cardiovascular and cerebrovascular effects

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical studies suggest that use of Ibuprofen, particularly at a high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200 mg/day) is associated with an increased risk of arterial thrombotic events.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided.

Careful consideration should also be exercised before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) particularly if high doses of ibuprofen (2400 mg/day) are required.

Renal Effects

Caution should be used when initiating treatment with Ibuprofen in patients with considerable dehydration.

As with other NSAIDs, long-term administration of Ibuprofen has resulted in renal papillary necrosis and other renal pathological changes. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependent reduction in prostaglandins formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those who are taking diuretics and ACE inhibitors and the elderly. 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. Discontinuation of NSAID drug therapy is usually followed by recovery to the pre-treatment state.

As NSAIDs can interfere with platelet function, and may prolong bleeding time, they should be used with caution in patients with intracranial haemorrhage and bleeding diathesis.

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

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, Undesirable effects*). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment.

Fenopine should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

As with other NSAIDs, ibuprofen may mask the signs of an infection.

Aseptic Meningitis

Aseptic Meningitis has been observed on rare occasions in patients with Ibuprofen therapy. Although it is probably more likely to occur in patients with systematic lupus erythematosus and related connective tissue disease, it has been reported in patients who do not have an underlying chronic disease.

4.5 Interaction with other medicinal products and other forms of interaction

Care should be taken in patients treated with any of the following drugs as interactions have been reported:

Antihypertensives: reduced antihypertensive effect

Diuretics: reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

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

Lithium: decreased elimination of lithium

Methotrexate: decreased elimination of methotrexate

Ciclosporin: increased risk of nephrotoxicity with NSAIDs

Other NSAIDs: avoid concomitant use of two or more NSAIDs

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding (*see section 4.4, Special warnings and precautions for use*).

Anticoagulants: NSAIDs may enhance the effects of anticoagulants such as warfarin, (*see section 4.4, Special warnings and precautions for use*).

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

Probenecid: there have been no reports of interactions between probenecid and ibuprofen. However, probenecid produces a reduction in metabolism and elimination of some NSAIDs and metabolites.

Oral hypoglycaemic agents: inhibition of metabolism of sulfonylurea drugs, prolonged half-life and increased risk of hypoglycaemia.

Care should be taken in the concomitant use of other protein binding drugs e.g. sulphonamides and hydantoins.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastro-intestinal bleeding (*see section 4.4, Special warnings and precautions for use*).

Ginkgo biloba may potentiate the risk of bleeding with NSAIDs.

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

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly.

Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

4.6 Fertility, pregnancy and lactation

Whilst no teratogenic effects have been demonstrated in animal toxicology studies, the use of ibuprofen during pregnancy should, if possible, be avoided.

Congenital abnormalities have been reported in association with ibuprofen administration in man; however, these are low in frequency and do not appear to follow any discernible pattern. In view of the known effects of NSAIDs on the foetal cardiovascular system (closure of ductus arteriosus), use in late pregnancy should be avoided.

In the limited studies so far available, ibuprofen appears in the breast milk in very low concentrations. Fenopine is not

recommended for use in nursing mothers

4.7 Effects on ability to drive and use machines

None Known.

4.8 Undesirable effects

Adverse reactions reported from extensive post-marketing experience are tabulated below by System Organ Class and frequency. The following convention has been utilised for the classification of undesirable effects: very common ($\geq 1/10$), common ($\geq 1/100$, $< 1/10$), uncommon ($\geq 1/1,000$, $< 1/100$), rare ($\geq 1/10,000$, $< 1/1,000$), very rare ($< 1/10,000$).

Gastrointestinal: 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, Special warnings and precautions for use*). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (*see section 4.4, Special warnings and precautions for use*) have been reported following administration. Less frequently, gastritis has been observed.

Hypersensitivity: Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, (very rare) bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis and erythema multiforme.

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

Clinical studies suggest that use of Ibuprofen, particularly at a high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (*see section 4.4, Special warnings and precautions for use*).

Other adverse events reported classed as uncommon and for which causality has not necessarily been established include:

Renal: Impaired renal function, renal nephrotoxicity in various forms, including interstitial nephritis, nephritic syndrome and renal failure.

Hepatic: Abnormal liver function, hepatitis and jaundice.

Neurological & special senses: Visual disturbances, optic neuritis, headache, paraesthesia, depression, confusion, hallucinations, tinnitus, vertigo, dizziness, malaise, fatigue and drowsiness.

Haematological: Thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia.

Dermatological: Photosensitivity (*see 'Hypersensitivity' for other skin reactions*).

Additional known side effects may occur rarely and include: hearing disturbances, haematuria may occur. Rarely impaired renal function may have been reported. Very rarely aseptic meningitis may occur.

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, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

The following signs and symptoms of overdose have been reported: headache, vomiting, drowsiness, loss of consciousness and hypotension. There is no specific antidote to Ibuprofen. Management usually includes gastric lavage associated with special care of plasma electrolytes and any other appropriate symptomatic relief.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Anti-inflammatory and anti-rheumatic products, non steroids.

ATC code: M01 AE01

Ibuprofen is a non-steroidal anti-inflammatory agent with analgesic and anti-pyretic activity. The analgesic activity of Ibuprofen is thought to be due to the inhibition of prostaglandin synthesis.

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

Ibuprofen is absorbed rapidly after oral administration, is strongly plasma protein bound, and is excreted mainly in urine as metabolites. The drug has a half life of 2 hours.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Pregelatinised maize starch
Colloidal anhydrous silica
Sodium Starch Glycolate (Type A)
Stearic Acid (HPMC)
Hypromellose (E464)
Talc
Titanium Dioxide (E171)
Erythrosin Aluminium Lake (E127)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original container.

6.5 Nature and contents of container

HDPE or Polypropylene containers with caps or child resistant closures in packs of 100, 250, 500 and 1000 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Limited
Trading as Pinewood Healthcare
Ballymacarbry
Clonmel
Co. Tipperary

8 MARKETING AUTHORISATION NUMBER

PA0281/088/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 04 June 1986

Date of last renewal: 22 December 2005

10 DATE OF REVISION OF THE TEXT

February 2016