

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen Seven Plus 200mg/5ml Oral Suspension

Pinofen Seven Plus 200 mg/5 ml Oral Suspension

Ibuprofen 200mg/5ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains 200mg of Ibuprofen.

Excipients:

Liquid Maltitol 4.25g/5ml

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral Suspension

4.1 Therapeutic indications

Children aged 7 to 12 years

Rheumatic or muscular pain, headache, dental pain, feverishness, symptoms of cold and influenza.

4.2 Posology and method of administration

For oral administration and short-term use only.

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

Children 7 to 12 years:

For children weighing more than 20kg, the daily dosage is 20mg/kg bodyweight in divided doses. Using the dosing device provided this can be achieved as follows;

7 to 9 years: 5 ml up to three times in 24 hours

10 to 12 years: 7.5ml up to three times in 24 hours

If in children aged 7 to twelve years this medicinal product is required for more than three days, or if symptoms worsen, a doctor should be consulted.

This product should only be given to children who weigh more than 20kg.

Leave at least four hours between doses and do not give more than the recommended amount in any 24 hours period.

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms (see section 4.4).

4.3 Contraindications

Hypersensitivity to ibuprofen or any of the excipients in the product.

Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema, or urticaria) in response to aspirin or other non-steroidal anti-inflammatory drugs.

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 NSAID therapy.

Severe heart failure, renal failure or hepatic failure (see section 4.4).

Last trimester of pregnancy (see section 4.6).

Children under seven years of age.

Children weighing less than 20kg.

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

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 section 4.2, GI and cardiovascular risks below)

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

Respiratory:

Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma or allergic disease.

Other NSAIDs:

The use of ibuprofen 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)

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

Renal tubular acidosis and hypokalaemia may occur following acute overdose and in patients taking ibuprofen products over long periods at high doses (typically greater than 4 weeks), including doses exceeding the recommended daily dose.

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 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). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. \leq 1200mg daily) 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.

Cases of Kounis syndrome have been reported in patients treated with Ibuprofen 200mg/5ml Oral Suspension. 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.

Impaired female fertility:

There is limited evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible upon withdrawal of treatment.

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.

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), and toxic epidermal necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), 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 ibuprofen in case of varicella (chickenpox).

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.

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

The label will include:

Read the enclosed leaflet before taking this product.

Do not give this product if your child:

Has (or has had two or more episodes of) a stomach ulcer, perforation or bleeding

Is allergic to ibuprofen or any other ingredient of the product, aspirin or other related painkillers

Is taking other NSAID painkillers, or aspirin with a daily dose above 75mg

Speak to a pharmacist or your doctor before taking if your child:

Has or has had asthma, diabetes, high cholesterol, high blood pressure, a stroke, heart, liver, kidney or bowel problems

Do not give to children aged 7-12 years for more than 3 days.

If symptoms persist or worsen, consult your doctor.

Do not exceed the stated dose.

Not recommended for children under 7 years.

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.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin 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 ibuprofen use (see section 5.1)

Other NSAIDs: including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects (see section 4.4).

Ibuprofen should be used with caution in combination with:

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

Antihypertensives and diuretics: NSAIDs may diminish the effect of these drugs. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

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 increase plasma glycoside levels.

Lithium: There is evidence for potential increase in plasma levels of lithium.

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

Ciclosporin: Increased risk of nephrotoxicity.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effects of mifepristone.

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

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 quinolones may have an increased risk of developing convulsions.

4.6 Fertility, pregnancy and lactation

Whilst no teratogenic effects have been demonstrated in animal experiments, the use of ibuprofen should, if possible, be avoided during the first six months of pregnancy.

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 trimester 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 trimester 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).

In limited studies, ibuprofen appears in the breast milk in very low concentration and is unlikely to affect the breast-fed infant adversely.

See section 4.4 regarding female fertility.

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

Hypersensitivity reactions have been reported and these may consist of:

- (a) non-specific allergic reactions and anaphylaxis

- (b) respiratory tract reactivity, e.g. asthma, aggravated asthma, bronchospasm, dyspnoea
- (c) various skin reactions, e.g. pruritis, urticaria, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme)

The following list of adverse effects relates to those experienced with ibuprofen at OTC doses, for short-term use. In the treatment of chronic conditions, under long-term treatment, additional adverse effects may occur.

Hypersensitivity reactions:

Uncommon: Hypersensitivity reactions with urticaria and pruritus.

Very rare: severe hypersensitivity reactions. Symptoms could be: facial tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension, (anaphylaxis, angioedema or severe shock).

Exacerbation of asthma and bronchospasm.

Gastrointestinal:

The most commonly-observed adverse events are gastrointestinal in nature.

Uncommon: abdominal pain, nausea, dyspepsia.

Rare: diarrhoea, flatulence, constipation and vomiting

Very rare: peptic ulcer, perforation or gastrointestinal haemorrhage, melaena, haematemesis, sometimes fatal, particularly in the elderly. Ulcerative stomatitis, gastritis.

Exacerbation of colitis and Crohn's disease (see section 4.4).

Nervous System:

Uncommon: Headache

Very rare: Aseptic meningitis – single cases have been reported very rarely.

Renal and urinary disorders:

Very rare: Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema

Not known: Renal tubular acidosis*.

Hepatic:

Very rare: liver disorders

Haematological:

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

Skin and subcutaneous tissue disorders:

Uncommon: various skin rashes

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

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

Immune system:

In patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease) during treatment with ibuprofen, single cases of symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been observed (see section 4.4).

Metabolism and Nutrition disorders:

Not known: Hypokalaemia*.

Cardiovascular and Cerebrovascular

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

Not known: Kounis syndrome.

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

* Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting typically following prolonged use of the ibuprofen component at higher than recommended doses.

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 at www.mhra.gov.uk/yellowcard.

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. Ringing in the ears, confusion, shaky eye movement, 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, agitation, somnolence, and disorientation or coma. Occasionally patients develop convulsions. At high doses, drowsiness, chest pain, palpitations, loss of consciousness, convulsions (mainly in children), weakness and dizziness, blood in urine, low levels of potassium in your blood, cold body feeling, and breathing problems have been reported. 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. Furthermore, there may be low blood pressure and reduced breathing.

Prolonged use at higher than recommended doses or overdose may result in renal tubular acidosis and hypokalaemia. Symptoms may include reduced level of consciousness and generalised weakness (see section 4.4 and section 4.8).

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 one 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.

5.1 Pharmacodynamic properties

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

ATC Code: M01 AE01

Ibuprofen is a propionic acid derivative NSAID that has demonstrated its efficacy by inhibition of prostaglandin synthesis. In humans ibuprofen reduces inflammatory pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits platelet aggregation.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within eight hours before or within 30 minutes after immediate release aspirin dosing (81mg), a decrease in the effect of aspirin 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 effects are considered to be likely for occasional ibuprofen use (see section 4.5).

5.2 Pharmacokinetic properties

Ibuprofen is rapidly absorbed following administration and is rapidly distributed throughout the whole body. The excretion is rapid and complete via the kidneys.

Maximum plasma concentrations are reached 45 minutes after ingestion if taken on an empty stomach. When taken with food, peak levels are observed after one to two hours. These times vary with different dosage forms.

The half-life of ibuprofen is about two hours.

In limited studies, ibuprofen appears in breast milk in very low concentrations.

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. 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, and 100 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

Shake well before use. Return any left over medicine to the Pharmacist for safe disposal.

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Ltd (trading as Pinewood Healthcare),

Ballymacarbry,

Clonmel,

Co. Tipperary, Ireland.

8 MARKETING AUTHORISATION NUMBER(S)

PL04917/0099

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/10/2024

10 DATE OF REVISION OF THE TEXT

22/11/2024