



Medicines & Healthcare products
Regulatory Agency



Ibuprofen Seven Plus 200mg/5ml Oral Suspension

Public Consultation

Proposal to make available from Pharmacies

The Medicines and Healthcare products Regulatory Agency (MHRA) is the UK government agency responsible for regulating medicines and medical devices. We continually review the safety of medicines and vaccines in the UK, and inform healthcare professionals and the public of the latest updates through several means, including public reclassification reports. Suspected side-effects to any drug or vaccine can be reported to MHRA by both healthcare professionals and members of the public via the Yellow Card Scheme (<http://www.mhra.gov.uk/yellowcard>)

Ref: ARM91

Ibuprofen Seven Plus 200mg/5ml Oral Suspension

Proposal to make available from Pharmacies without prescription

We want to know what you think

- Ibuprofen Seven Plus 200mg/5ml Oral Suspension is used for the relief of certain types of pain and for the symptoms of colds and influenza.
- Ibuprofen Seven Plus is only at the moment available on prescription.
- We propose to make it available in pharmacies.
- At the moment all oral suspensions of ibuprofen available without prescription are half the strength of Ibuprofen Seven Plus (100mg /5ml)
- The Commission on Human Medicines advised that this product can be available as a Pharmacy medicine.
- We want to know what you think about this change.

Please tell us your views – please use the form at the end of this document.

The deadline for comments is **4 April 2016**.

In this document there is:

- A summary of the proposed change and the background
- A copy of the patient information leaflet and label proposed if the change goes ahead
- A form for your response

The full name of the medicine is Ibuprofen Seven Plus 200mg/5ml Oral Suspension – in this document, we will call it 'Ibuprofen Seven Plus'

Contents:

1. Background about deciding where medicines are available
2. About Ibuprofen Seven Plus
3. Proposal to make Ibuprofen Seven Plus available as a Pharmacy medicine
4. How was the proposal assessed for Ibuprofen Seven Plus being available as a Pharmacy medicine?
5. Further details on the application
6. What do you think?

Product details:

Product name: Ibuprofen Seven Plus 200mg/5ml Oral Suspension

Active substances: Ibuprofen

Licence holder: Pinewood Laboratories Limited

Route of sale/supply: Current – on prescription (POM); Proposed – Pharmacy (P)

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

Marketing Authorisation Number: PL 04917/0099

Consultation is open from: 15 March 2016 – 4 April 2016

Reference: ARM91

Contact: reclassification@mhra.gsi.gov.uk

1. Background on deciding where medicines are available

The role of MHRA

MHRA regulates medicines and medical devices in the UK, on behalf of the UK Licensing Authority. This means that MHRA decides whether medicines are available:

- on prescription only - 'prescription only medicine' (POM)
- bought from pharmacies - 'pharmacy medicine' (P)
- bought from other shops - 'general sales list medicine' (GSL)

What is re-classification of a medicine?

Making a change on where a medicine is available is called 're-classification'. This is sometimes referred to as 'switching'. To decide on this change, MHRA may:

- take advice from its committees of external experts
- take advice from a group ('stakeholder group') of health professionals and representatives of people affected by the classification change
- run a public consultation

To be reclassified from POM to P, a medicine must:

- be unlikely to be a direct or indirect danger to human health when used without the supervision of a doctor, even if used correctly
- be generally used correctly (ie not frequently or to a wide extent used correctly)
- not contain substances or preparations of substances where the activity of the product or its side effects require further investigation
- not normally be prescribed by a doctor for injection (parenteral administration)

What evidence is needed?

A company or organisation can ask MHRA for a medicine to be available as a pharmacy medicine or a general sale medicine. To do this, they need to get together evidence to show that the medicine

- a) is likely to be used appropriately, and
- b) with relatively little danger to the public.

This evidence needs to focus on the risk to the public. This includes evidence on the possible abuse or misuse of the medicine. The evidence may include:

- clinical studies
- evidence showing acceptable level of side effects
- advice of experts
- views of relevant health professionals and their professional bodies
- views of relevant public associations and individuals with an interest in the medicine under consideration.

Who makes the final decision?

The final decision on whether to approve a change is made by the MHRA, on behalf of the UK Licensing Authority.

2. About Ibuprofen Seven Plus

Ibuprofen Seven Plus 200mg/5ml Oral Suspension is a medicine for rheumatic or muscular pain, headache, dental pain, feverishness, symptoms of cold and influenza. It can be used in children aged 7-12 years. This medicine is currently a Prescription Only Medicine.

The Commission on Human Medicines has advised that this product can be available as a Pharmacy medicine. This report outlines the background to this decision. Please tell us your views

by using the response form at the end of this document (Annex 1). The deadline for comments is **4 April 2016**.

The patient information leaflet and label are provided in Annex 2 and 3.

What is in Ibuprofen Seven Plus?

Ibuprofen Seven Plus is an oral suspension containing 200mg ibuprofen in 5ml.

This is the first application for a liquid ibuprofen product at 200mg/5ml strength to be available without prescription. Only one strength of liquid ibuprofen has ever been available in the UK without prescription – 100mg/5ml.

What is ibuprofen used for?

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID). It is currently available from several companies as a suspension, tablets, powders and granules as Prescription only medicine, a Pharmacy medicine or a General Sales List medicine. . As a Pharmacy or General Sales list medicine it is used to reduce pain and fever in both adults and children. Further details of these conditions are provided below -

Ibuprofen is available as a GSL medicine under the following conditions:

Tablets, capsules, powders, granules

- Maximum strength: 200mg

-For rheumatic or muscular pain, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness, symptoms of colds and influenza.

-Adults and children over 12.

Max dose: 400mg, Max daily dose : 1200mg

Max pack : 16 tabs or caps, 12 sachets of powder or granules

Liquid

Max strength 2% (100mg in 5ml).

For the treatment of rheumatic or muscular pain, headache, dental pain, feverishness, or symptoms of colds and influenza.

For children under the age of 12 years

Max dose: 200mg. Max daily dose: 800mg.

Max pack: Individual unit doses of not more than 5ml each in a pack containing not more than 20 doses or

Multidose containers containing not more than 100ml of product.

Ibuprofen is available as a Pharmacy medicine under the following conditions:

- For rheumatic and muscular pain, pain of non-serious arthritic conditions, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea , feverishness, symptoms of colds and influenza.

- Maximum dose: 400mg (600mg for prolonged release preparations)

- Maximum daily dose: 1,200mg.

3. Proposal to make Ibuprofen Seven Plus available as a Pharmacy medicine

Who has made the proposal?

The licence-holder for Ibuprofen Seven Plus (Pinewood Laboratories Limited) has applied to make this product available through Pharmacies.

What is the view of the Commission on Human Medicines?

The Commission on Human Medicines has advised that this product can be available as a Pharmacy medicine. Advice was also received from the Patient and Public Engagement Expert Advisory Group on improvements to the leaflet and label. The Patient and Public Engagement Expert Advisory Group's remit includes advising the Commission on Human Medicines on the development of effective communications for patients.

What are the details of this change?

The application proposes to make Ibuprofen Seven Plus available through Pharmacy outlets for:

- Oral use
- Strength: 200mg/5ml Ibuprofen
- For use in children between 7 and 12 years
- To treat rheumatic or muscular pain, headache, dental pain, feverishness, symptoms of cold and influenza.
- Dose: for Children aged 7-9 years: 5ml (200mg) three times daily;
for Children aged 10-12 years: 7.5ml (300mg) three times daily.
- Maximum length of treatment: 3 days.
- Maximum pack size: 100ml.

4. How was the proposal assessed for Ibuprofen Seven Plus being available on as a Pharmacy medicine?

To be reclassified from POM to P, a medicine must:

- be unlikely to be a direct or indirect danger to human health when used without the supervision of a doctor, even if used correctly
- be generally used correctly (ie not frequently or to a wide extent used correctly)
- not contain substances or preparations of substances where the activity of the product or its side effects require further investigation
- not normally be prescribed by a doctor for injection (parenteral administration)

These criteria are set out in the Human Medicines Regulations 2012, regulation 62(3).

Assessment of suitability for Pharmacy availability

The MHRA assessed the application against these criteria for reclassification:

Direct danger

It is considered that ibuprofen is well established in the P and GSL setting and the risks of direct danger are no greater than other liquid ibuprofen products. "Direct danger" means that a danger may be present if the product causes adverse reactions that are important. The dose, age range, use and pack size for this product are all within accepted parameters for other liquid ibuprofen products available as Pharmacy medicines.

Indirect danger

It is accepted that ibuprofen is already available in both P and GSL settings, for treatment of the listed conditions in children. There are no additional indirect risks in this regard which arise from the active ingredient, ibuprofen. "Indirect dangers" are considered to be when treatment might mask an underlying condition that requires medical attention.

However, there is considered to be a risk of confusing the 200mg/5ml product with all other ibuprofen suspension products which are already available without prescription - which are half the strength (100mg/5ml). The risk is that a parent/carer, who may be used to giving quantities of suspension suitable for the 100mg/5ml product, might give twice the dose to a child if they give the same amount of this product.

The company has proposed appropriate risk minimisation measures to manage the risk of confusion. This will be done by clear warnings on the leaflet and label, and by adding the words, "double strength" clearly highlighted to the outer box and to the label on the bottle itself. Additionally as a P medicine this product will be supplied only from pharmacies under the supervision of a pharmacist and therefore pharmacy staff can provide additional advice on correct

use. The company will ensure pharmacy staff are made aware of this product being twice the normal strength via a Dear Healthcare Professional letter, a letter produced by the company to alert healthcare professionals of important safety warnings and messages for medicines.

Incorrect use – frequently and to a very wide extent

There is no evidence that any ibuprofen products are frequently and to a very wide extent used incorrectly.

Activity and/or adverse reactions require further investigation

This medicinal product contains only ibuprofen as the active ingredient. The activity of and adverse reactions to ibuprofen are well known.

Is normally prescribed as an injection

This product is for oral use only, so this criterion does not apply.

5. Further details on the application

Risk Management Plan

The application contains a risk management plan (RMP). RMPs are documents that contain information on a medicine's safety profile and one or more of the following:

- how any risks identified in the safety profile will be prevented or minimised in patients
- plans for studies and other activities to gain more knowledge about the safety and efficacy of the medicine
- risk factors for side effects
- measuring the effectiveness of measures taken to prevent or minimise risks.

The RMP for this product has identified the main risk to be pharmacists and/or parents/carers confusing it with the 100mg/5ml ibuprofen liquid products, which are half the strength. This risk has been minimised by clear warnings on the leaflet and label. Also, as the product will be classified as a Pharmacy medicine additional advice on correct use will also be available from the pharmacy staff.

Label and leaflet

The patient information leaflet and label are provided in Annex 2 and 3.

Summary of Product Characteristics

The Summary of Product Characteristics, is provided in Annex 4. This document is a description of Ibuprofen Seven Plus's properties and the conditions attached to its use. It is used as a reference by healthcare professionals.

6. What do you think?

- **Ibuprofen Seven Plus 200mg/5ml Oral Suspension is used for the relief of certain types of pain and for the symptoms of colds and influenza.**
- **Ibuprofen Seven Plus is only at the moment available on prescription.**
- **We propose to make it available in pharmacies.**
- **The Commission on Human Medicines advised that this product can be available as a Pharmacy medicine.**
- **We want to know what you think about this change.**

Please tell us your views – please use the form on the next page in Annex 1. Please respond by 4 April 2016.

Your details

Name:

Position (if applicable):

Organisation (if applicable):

Email:

1. Do you consider that Ibuprofen Seven Plus should be available as a Pharmacy medicine?

Yes No Not sure

Please provide any comments or evidence to support your response:

2. Do you have any specific comments on the leaflet or the label provided in the public reclassification report for Ibuprofen Seven Plus?

3. Do you have any other comments on the reclassification?

4. The MHRA may publish consultation responses. Do you want your response to remain confidential?

Yes Partially* No

*If partially, please indicate which parts you wish to remain confidential. In line with the Freedom of Information Act 2000, if we receive a request for disclosure of the information we will take full account of your explanation, but we cannot give an assurance that confidentiality can be maintained in all circumstances. Responses to consultation will not normally be released under FOI until the regulatory process is complete.

Responses can be continued onto a separate page if required. This form should be returned by email (reclassification@mhra.gsi.gov.uk) to arrive by **4 April 2016**. Contributions received after that date cannot be included in the exercise.

Effective relief from aches, pain and fever in children from seven to twelve years.
 Do not use for children under 7 years.
 Each 5 ml of oral suspension contains 200 mg ibuprofen. Also contains: E965 and sodium benzoate.
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 ingredients of the product, aspirin or other related painkillers
- Is taking other NSAID painkillers, or aspirin with a daily dose above 75 mg.

Speak to a pharmacist or your doctor before giving this product to your child if he or she:

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

Children from 7 to 12 years
SEVEN PLUS
Ibuprofen
200 mg/5 ml
ORAL SUSPENSION
Double Strength
 Sugar & colour free
Strawberry flavour
80 ml **7+**

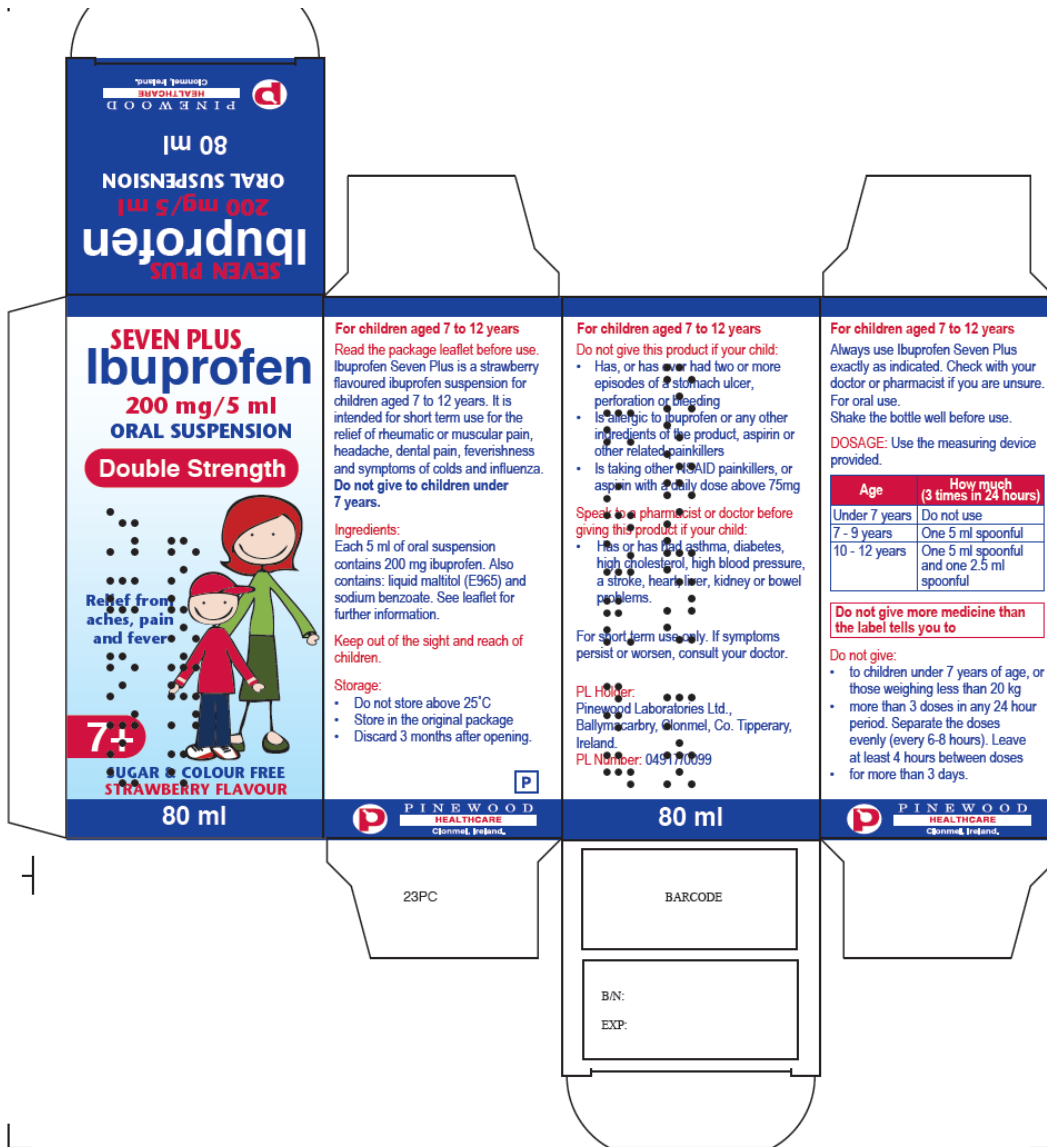
For short term use only. If symptoms persist or worsen, consult your doctor.
 Do not store above 25°C.
 PL Holder: Pinewood Laboratories Ltd, Ballymacarby, Clonmel, Co. Tipperary, Ireland.
 PL04917/0099 23LL **P**

Read the package leaflet before use.
 For oral use. Shake the bottle well before use.
 Dosage: use the measuring device provided.

| Age | How much (3 times in 24 hours) |
|---------------|---|
| Under 7 years | Do not use |
| 7 - 9 years | One 5 ml spoonful |
| 10 - 12 years | One 5 ml spoonful and one 2.5 ml spoonful |

Do not give more than 3 doses in any 24 hour period. Separate the doses evenly (every 6-8 hrs). Do not give to children aged 7-12 years for more than 3 days.
Do not exceed the stated dose.
 Keep out of the sight and reach of children.

B/N:
EXP:



Package leaflet: Information for the user

Ibuprofen 200 mg/5 ml Seven Plus Oral Suspension

Read all of this leaflet carefully before you start using this medicine because it contains important information for you and your child.

Your medicine is called Ibuprofen 200mg/5ml Seven Plus Oral Suspension. It will be referred to throughout this leaflet as "Ibuprofen Seven Plus".

This medicine is available without prescription, but you still need to give Ibuprofen Seven Plus carefully to get the best results from it. Always use this medicine exactly as described in this leaflet or as your doctor or pharmacist has told you.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- If you get any side effects, talk to your pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- You must talk to your doctor if your child does not feel better or feels worse after three days.

What is in this leaflet:

1. What Ibuprofen Seven Plus is and what it is used for
2. What you need to know before you give Ibuprofen Seven Plus
3. How to give Ibuprofen Seven Plus
4. Possible side effects
5. How to store Ibuprofen Seven Plus
6. Contents of the pack and other information

1. What Ibuprofen Seven Plus is and what it is used for

Ibuprofen Seven Plus contains Ibuprofen as the active ingredient. Each 5 ml of oral suspension contains 200 mg of ibuprofen. **This is twice the strength of normal ibuprofen suspension and you should be careful that you use the correct dose.**

Ibuprofen belongs to a group of medicines called non-steroidal anti-inflammatory drugs (NSAIDs).

Ibuprofen Seven Plus is given to children aged 7 - 12 years as a painkiller for relief of mild to moderate muscular pain, headache and dental pain. It also reduces the temperature in fever and relieves the symptoms of colds and influenza.

This medicine is intended for short term use in children aged 7 - 12 years.

2. What you need to know before you give Ibuprofen Seven Plus

Do NOT give this medicine if your child:

- has an allergy or hypersensitivity to ibuprofen or any of the other ingredients in this medicine (*see Section 6 and Section 2: Important information about ingredients*)
- has had an allergic reaction such as wheezing, an asthma attack, runny nose, skin reaction or swelling after taking aspirin or other non-steroidal anti-inflammatory painkillers
- has ever had a stomach ulcer or a history of bleeding into, or perforation of, the intestine especially after previous NSAID treatment
- is taking any other non-steroidal anti-inflammatory painkillers (NSAIDs) such as naproxen.
- is taking aspirin at doses above 75 mg daily
- has ever had severe kidney, heart or liver problems
- is suffering from severe dehydration
- has an inherited intolerance to some sugars
- is less than seven years of age or weighs less than 20 kg.

Warnings and precautions

You should discuss your child's treatment with your doctor or pharmacist before giving this medicine if your child:

- has kidney, liver or bowel problems
- has lupus (SLE) or mixed connective tissue disease
- has a chronic inflammatory bowel disease such as ulcerative colitis or Crohn's disease

- has asthma or allergic diseases of the lungs
- has chickenpox

If any of these apply, ask for advice from a doctor or pharmacist before using this medicine.

Medicines such as Ibuprofen Seven Plus may be associated with a small increased risk of heart attack ("myocardial infarction") or stroke. Any risk is more likely with high doses and prolonged treatment.

Do not exceed the recommended dose or duration of treatment.

There is a risk of renal (kidney) impairment in dehydrated children.

Drinking alcohol while taking ibuprofen may increase the risk of certain side effects.

Other medicines and Ibuprofen Seven Plus

Please tell your doctor or pharmacist if your child is taking, has recently taken or might take any other medicines, including medicines obtained without a prescription. Ibuprofen Seven Plus may affect or be affected by some medicines. For example:

- Any other ibuprofen preparations or NSAID painkillers, including those you can buy without a prescription.
- Aspirin
- Medicines that are anticoagulants (i.e. thin blood/ prevent clotting, e.g. aspirin, warfarin)
- Medicines that reduce high blood pressure (ACE inhibitors such as captopril, beta-blockers such as atenolol, angiotensin-II receptor antagonists such as losartan)
- Cardiac glycosides (used in the treatment of heart problems, such as digoxin)
- Ciclosporin or tacrolimus (used to suppress the body's immune system)
- Corticosteroids (anti-inflammatory drugs, such as prednisolone or beclomethasone.)
- Diuretics (to help pass water such as furosemide or bendroflumethiazide)
- Lithium, or selective serotonin reuptake inhibitors (SSRIs such as fluoxetine - used to treat mood disorders)
- Methotrexate (used to treat rheumatoid arthritis, psoriasis and some cancers)
- Mifepristone (used to terminate pregnancy)
- Quinolone antibiotics (used to treat a wide range of infections e.g. Ciprofloxacin)
- Zidovudine (used to treat HIV)

Some other medicines may also affect or be affected by the treatment of Ibuprofen Seven Plus. You should therefore always seek the advice of your child's pharmacist or doctor before you give Ibuprofen Seven Plus with other medicines.

Important information about some of the ingredients of this medicine:

- Maltitol (E965) may have a mild laxative effect (calorific value 2.3 kcal/g). If you have been told that you or your child has an intolerance to some sugars, contact your doctor before taking/giving this medicine.

If you are an adult taking this medicine, the warnings and information given in this section apply and in addition the following:

- ibuprofen belongs to a group of medicines which may impair fertility in women. This is reversible on stopping the medicine. It is unlikely that this medicine, used occasionally, will affect your chances of becoming pregnant, however, tell your doctor before taking this medicine if you have problems becoming pregnant
- you should only take this product on a doctor's advice during the first 6 months of pregnancy
- DO NOT take this medicine if you are in the last 3 months of your pregnancy
- in limited studies, ibuprofen appears in the breast milk in very low concentration and is unlikely to affect the breast-fed infant adversely
- medicines such as Ibuprofen Seven Plus may be associated with a small increased risk of heart attack ("myocardial infarction") or stroke. Any risk is more likely

with high doses and prolonged treatment. Do not exceed the recommended dose or duration of treatment

- You should discuss your treatment with your doctor or pharmacist if you have diabetes, high cholesterol, high blood pressure, heart problems including heart failure, angina (chest pain), or if you have had a heart attack, bypass surgery, peripheral artery disease (poor circulation in the legs or feet due to narrow or blocked arteries), or any kind of stroke (including 'mini stroke' or transient ischaemic attack 'TIA'), or if you have a family history of heart disease or stroke, or if you are a smoker.
- If you are elderly talk to your doctor before using this medicine. Some of the ingredients can cause problems.

Driving and using machines

Ibuprofen Seven Plus is not expected to affect your ability to drive or operate machinery.

3. How to give Ibuprofen Seven Plus

This product is twice the strength of normal ibuprofen suspension and you should be careful that you use the correct dose.

Always use Ibuprofen Seven Plus exactly as described in this leaflet or as your doctor or pharmacist has told you. Check with your doctor or a pharmacist if you are unsure. Shake the bottle well before measuring the dose. A measuring device is provided to ensure accuracy.

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

| Age | How Much |
|--|---|
| Under seven years | Do not use |
| Seven - nine years | One 5 ml spoonful up to three times in 24 hours |
| Ten - twelve years | One 5 ml spoonful and one 2.5 ml spoonful up to three times in 24 hours |
| <ul style="list-style-type: none"> • Do not give to children under 7 years of age, or those weighing less than 20 kg • Separate the doses evenly (every 6-8 hours). Leave at least 4 hours between doses. • Do not give more than 3 doses in any 24 hour period. | |

Warning: Do not exceed the stated dose

If your child's symptoms persist for more than three days, consult a doctor.

If you give more medicine than you should - If your child takes more than the stated dose (an overdose), you should contact a doctor immediately, or go to the nearest hospital casualty department, and take the bottle with you if you can.

If you forget to give this medicine - If you forget to give a dose, give it as soon as you remember, unless it is almost time for the next dose. Do not give a double dose to make up for the missed dose.

For oral use only.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible Side Effects

Like all medicines, ibuprofen can cause side-effects, although not everybody gets them. The most common side-effect is irritation of the stomach which can cause problems in some patients.

If any of the following occur, stop giving the medicine and seek immediate medical help:

- Passing blood in the stools (faeces/motions)
- Passing black tarry stools
- Vomiting blood or dark particles that look like coffee grounds
- Unexplained wheezing, shortness of breath, skin rash (which may be severe and include blistering or peeling of the skin), itching or bruising, light-headedness, racing of the heart or fluid retention e.g. swollen ankles, not passing enough water

- stiff neck, headache, nausea, vomiting, fever and disorientation
- swelling of the face.

If any of the following occur, stop giving the medicine and tell your doctor:

- If your child's skin starts to turn red or if they develop a painful skin reaction or their skin starts to blister or peel - this is very rare
- Unexplained stomach pain, indigestion, heartburn, feeling sick and/or vomiting
- Yellowing of the eyes and/or skin
- Severe sore throat with high fever or unexplained bleeding, bruising and tiredness.

Other unusual effects may include the following:

Uncommon:

- Headache, dizziness, sleeplessness, agitation, irritability or tiredness
- Visual disturbances

Rare:

- Flatulence, diarrhoea or constipation
- Ringing in the ears (tinnitus)
- Kidney damage, increased blood uric acid levels.

Very Rare:

- Occasionally hypersensitivity reactions may occur which can cause skin rashes as well as asthma attacks, swelling of the tongue and breathlessness
- Liver problems may occur with ibuprofen
- Passing less urine than normal, increased proteins in the blood (detected by tests)
- Crohn's disease or ulcerative colitis or other stomach problems may be exacerbated
- Depression or psychotic reactions
- Hair loss
- High blood pressure.

Reporting of side effects:

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Ibuprofen Seven Plus

Keep this medicine out of the sight and reach of children. Do not use this medicine after the expiry date, which is shown on the bottle. The expiry date refers to the last day of that month. Do not store above 25°C. Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away any medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and further information

What Ibuprofen Seven Plus contains:

Each 5ml contains 200mg of the active ingredient ibuprofen. The other ingredients are: glycerol (E422), xanthan gum, liquid maltitol (E965), polysorbate 80, saccharin sodium (E954), citric acid monohydrate, sodium benzoate (E211), magnesium aluminium silicate, purified water and strawberry flavour (contains propylene glycol).

What Ibuprofen Seven Plus looks like and contents of the pack:

Ibuprofen Seven Plus is a colour-free, white oral suspension. This medicine comes in amber glass bottles containing 70 ml, 80 ml or 100 ml with a child-resistant closure. Not all pack sizes may be marketed. A double ended spoon with measures of 1.25 ml, 2.5 ml and 5 ml is provided.

This medicine should be used within three months of first opening.

Marketing Authorisation Holder
Pinewood Laboratories Ltd., Ballymacarbray, Clonmel, Co. Tipperary, Ireland.

Manufacturer
Pinewood Laboratories Ltd., Ballymacarbray, Clonmel, Co. Tipperary, Ireland.
PL Number: 04917/0099

This leaflet was last updated in February 2016

SUMMARY OF PRODUCT CHARACTERISTICS

Annex 4

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen Seven Plus 200mg/5ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITIONS

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 CLINICAL PARTICULARS

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. The patient should consult a doctor if symptoms persist or worsen, or if the product is required for more than ten days.

Leave at least four hours between doses and do not take more than 1200mg in any 24 hour period.

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)

Elderly:

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.

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. ≤ 1200 mg 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.

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.

Dermatological:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Ibuprofen 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 (chickenpox).

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 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: 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 or heparin (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.

4.6.1 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.

During the 3rd trimester, ibuprofen is contraindicated as there is a risk of premature closure of the fetal ductus arteriosus with possible persistent pulmonary hypertension. The onset of labour may be delayed and the duration increased with an increased bleeding tendency in both mother and child (see section 4.3).

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.

4.6.2 Effects on ability to drive and use machines

None expected at recommended dose and duration of therapy

4.6.3 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 |

Hypersensitivity reactions have been reported and these may consist of:

- (a) non-specific allergic reactions and anaphylaxis
- (b) respiratory tract reactivity, eg 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:

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

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.

Dermatological:

Uncommon: various skin rashes

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

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).

Cardiovascular and Cerebrovascular

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

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).

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.

4.6.3.1.1 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 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 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 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 competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamics studies show that when single doses of ibuprofen 400mg were taken within eight hours before or within 30 minutes after immediate release acetylsalicylic acid

(aspirin) dosing (81mg), a decreased effect of aspirin 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 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

24 months

In use shelf life: 3 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 Safe Disposal

Shake well before use. Return any leftover medicine to the pharmacist for safe disposal.

7. Marketing Authorisation Holder

Pinewood Laboratories Limited

Ballymacarbary

Clonmel

Co. Tipperary

Ireland

8. Marketing Authorisation Number

PL04917/0099

9. Date of First Authorisation / Renewal of Authorisation

20/10/2011

10. Date of Revision of the Text