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**LAY SUMMARY**

On 20th October 2011, the MHRA granted Pinewood Laboratories Limited Marketing Authorisations (licences) for Ibuprofen Seven Plus 200 mg/5 ml Oral Suspension and Ibuprofen 200 mg/5 ml Oral Suspension.

Ibuprofen Seven Plus/Ibuprofen 200 mg/5 ml Oral Suspension contains the active ingredient ibuprofen.

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

Ibuprofen Seven Plus 200 mg/5 ml Oral Suspension is used in children aged 7 to 12 years for rheumatic or muscular pain, headache, dental pain, feverishness, symptoms of cold and influenza.

Ibuprofen 200 mg/5 ml Oral Suspension is given to children under 12 as a painkiller for relief of mild to moderate muscular pain, headache, teething pain and toothache. It also reduces the temperature in fever (e.g. colds, influenza and post-immunisation fever).

For adults and children over 12 it can also be used for backache, migraines, neuralgia and relief from non-serious arthritic conditions.

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Ibuprofen Seven Plus/Ibuprofen 200 mg/5 ml Oral Suspension outweigh the risks; hence these Marketing Authorisations have been granted.
IBUPROFEN SEVEN PLUS 200 mg/5 ml ORAL SUSPENSION

IBUPROFEN 200 MG/5 ML ORAL SUSPENSION

PL 04917/0099 AND 0121

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted Marketing Authorisations for the medicinal products Ibuprofen Seven Plus 200 mg/5 ml Oral Suspension and Ibuprofen 200 mg/5 ml Oral Suspension (PL 04917/0099 and 0121) to Pinewood Laboratories Limited on 20th October 2011. Ibuprofen Seven Plus 200 mg/5 ml Oral Suspension is obtained from a pharmacy and is indicated in children aged 7 to 12 years for rheumatic or muscular pain, headache, dental pain, feverishness, symptoms of cold and influenza.

Ibuprofen 200 mg/5 ml Oral Suspension is available with a prescription only (POM) and is indicated in children under 12 years of age for rheumatic or muscular pain, headache, dental pain, feverishness (including post-immunisation pyrexia), symptoms of cold and influenza. It is also indicated in children over 12 years for rheumatic or muscular pain, pain of non-serious arthritic conditions, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness, symptoms of colds and influenza.

These applications are submitted as abridged applications according to Article 10.3 of Directive 2001/83/EC, claiming to be a hybrid medicinal product to Nurofen 200 mg Tablets (PL 00327/0146) authorised to Crookes Healthcare Limited on 15th July 2003. This licence then underwent a change of ownership to Reckitt Benckiser Healthcare (UK) Limited on 29th January 2011 (PL 00063/0385). This was a line extension of the original Marketing Authorisation, first authorised to Crookes Healthcare Limited on 6th May 1983 (PL 00327/0004).

Ibuprofen, which is a propionic acid derivative, is a non-steroidal anti-inflammatory drug (NSAID) which has well established analgesic and antipyretic properties.

The pharmacovigilance system as described by the applicant fulfils the requirements. It also provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring.

A satisfactory justification for the absence of a Risk Management Plan (RMP) has been provided.
**PHARMACEUTICAL ASSESSMENT**

**DRUG SUBSTANCE**

INN: Ibuprofen  
Chemical name: \((2RS)-2-[4\text{-}methyl\text{-}propyl]phenyl\)propanoic acid.

Structure:

![Structure diagram](image)

Physical form: white or almost white crystalline powder.  
Solubility: practically insoluble in water, freely soluble in acetone, in methanol and in dichloromethane. It dissolves in dilute solutions of alkali hydroxides and carbonates.

Molecular formula: \(C_{13}H_{18}O_2\)  
Molecular weight: 206.3

Ibuprofen is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture of the drug substance from its starting materials are controlled by Certificates of Suitability.

All potential known impurities have been identified and characterised.

An appropriate specification with suitable test methods and limits is provided for the drug substance. The methods of testing and limits for residual solvents are in compliance with current guidelines. Batch analysis data are provided and comply with the proposed specification.

The proposed retest period is in-line with the Certificate of Suitability and is satisfactory.

**DRUG PRODUCT**

Other ingredients

Other ingredients consist of the pharmaceutical 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) and purified water.

All the ingredients with the exception of strawberry flavour comply with their relevant European Pharmacopoeia monographs. Strawberry flavour complies with in-house specifications.

None of the excipients used contain material of animal or human origin.
Pharmaceutical Development
The objective of the development programme was to produce an acceptably tasting product which contained 200mg of ibuprofen in 5mL. Development of this strength of product has been based on the applicant’s 100mg/5mL product.

The applicant has provided a suitable product development section. Justifications for the use and amounts of each excipient have been provided and are valid.

The reference product used in the bioequivalence study is Nurofen 200 mg Tablets, authorised in Ireland to Reckitt Benckiser Ireland Limited. This is considered to be pharmaceutically equivalent to the UK reference product.

Manufacturing Process
A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results. Satisfactory process validation data on pilot-scale batches have been provided. The applicant has committed to perform process validation on future commercial-scale batches.

Finished product specification
The finished product specification is satisfactory. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of Analysis for any working standards used have been provided.

Container-Closure System
The product is packaged in amber bottles sealed with child-resistant, tamper evident caps. A double-ended spoon with measures of 1.25 ml, 2.5 ml or 5 ml is provided.

The pack sizes are 60 ml, 80 ml, 100 ml, 150 ml and 200 ml.

Specifications and Certificates of Analysis have been provided. All primary product packaging complies with EU legislation regarding contact with food.

Stability of the product
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf life for the unopened product of 24 months and an in-use shelf-life of 3 months has been set. Storage instructions are: ‘Do not store above 25°C. Store in the original pack’. This is satisfactory.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL), Labels
The SmPCs, PIL and labelling are pharmaceutically acceptable.

Patient Information Leaflet (PIL)
This is pharmaceutically satisfactory.
User testing results have been provided for approved product Ibuprofen 100 mg/5 ml Paediatric Oral Suspension BP, which was originally approved to McNeil Products Limited (PL 15513/0119). This licence underwent a change of ownership to Pinewood Laboratories Limited on 30th September 2005 (PL 04917/0080). The results indicate that the PIL is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.
UKPAR Ibuprofen Seven Plus/Ibuprofen 200 mg/5 ml Oral Suspension PL 04917/0099 and 0121

As the PIL for this is similar to the PIL for Ibuprofen 200 mg/5 ml Oral Suspension, this is satisfactory.

**MAA Form**
These are pharmaceutically satisfactory.

**Expert report**
The pharmaceutical expert report has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical dossier.

**Conclusion**
It is recommended that Marketing Authorisations are granted for these applications from a quality point of view.
NON-CLINICAL ASSESSMENT

The pharmacodynamics, pharmacokinetics and toxicological properties of ibuprofen are well-known. As ribavirin is a widely used, well-known active substance, the applicant has not provided any new non-clinical data and none are required. An overview based on literature review is, thus, appropriate.

No new non-clinical data have been supplied with these applications and none are required for applications of this type.

A satisfactory justification for the absence of an Environmental Risk Assessment has been provided.

It is recommended that a Marketing Authorisation is granted for these applications from a non-clinical point of view.
CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY
To support these applications, the Marketing Authorisation Holder has included a bioequivalence study:

An open-label, randomised, single-dose, two-way crossover, comparative bioequivalence study, comparing the pharmacokinetics of Ibuprofen 200 mg/5 ml Oral Suspension (Test) versus Nurofen (ibuprofen) 200 mg Tablets (Reference) in healthy volunteers under fasting conditions.

Blood samples were taken pre- and up to 12 hours post dose. There was a minimum washout period of 48 hours between each treatment period. Pharmacokinetic parameters were measured from the plasma and statistically analysed.

Results for ibuprofen are presented below as log-transformed values:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>( \text{AUC}_{0-t} ) (( \mu \text{g/ml.h} ))</th>
<th>( \text{AUC}_{0-\infty} ) (( \mu \text{g/ml.h} ))</th>
<th>( \text{C}_{\text{max}} ) (( \mu \text{g/ml} ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test (T)</td>
<td>55.66</td>
<td>57.90</td>
<td>17.31</td>
</tr>
<tr>
<td>Reference (R)</td>
<td>59.20</td>
<td>61.29</td>
<td>18.28</td>
</tr>
<tr>
<td>T/R Ratio</td>
<td>94.01</td>
<td>94.48</td>
<td>94.69</td>
</tr>
<tr>
<td>(90% CI)</td>
<td>88.99 – 99.33</td>
<td>89.56 – 99.66</td>
<td>84.35 – 106.30</td>
</tr>
</tbody>
</table>

The results for the primary variables indicated that the 90% confidence intervals test/reference ratio of geometric means for \( \text{AUC}_{0-t} \) and \( \text{C}_{\text{max}} \) for ibuprofen lie within acceptable limits (80%-125%). Thus, bioequivalence has been shown between the test and reference products in this study.

EFFICACY
No new efficacy data were submitted with this application and none were required.

SAFETY
With the exception of the data submitted during the bioequivalence study, no new safety data were submitted with this application and none were required. No new or unexpected safety concerns were raised during the bioequivalence study.

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC), PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
The SmPCs, PIL and labelling are clinically satisfactory and consistent with those for the reference product, where appropriate.

CLINICAL EXPERT REPORT
The clinical expert report has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.
MAA FORM
The MAA forms are clinically satisfactory.

CONCLUSIONS
It is recommended that Marketing Authorisations are granted for these applications from a clinical point of view.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Ibuprofen Seven Plus/Ibuprofen 200 mg/5 ml Oral Suspension are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL
No new non-clinical data have been supplied with these applications and none are required for applications of this type.

EFFICACY
Bioequivalence has been demonstrated between the applicant’s Ibuprofen 200 mg/5 ml Oral Suspension and the reference product Nurofen 200 mg Tablets.

Ibuprofen Seven Plus/Ibuprofen 200 mg/5 ml Oral Suspension can be considered a hybrid medicinal product to Nurofen 200 mg Tablets.

No new or unexpected safety concerns arise from these applications.

The SmPCs, PIL and labelling are satisfactory and consistent with those for the reference product.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant’s product and the reference product are interchangeable. Extensive clinical experience with ibuprofen is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.
IBUPROFEN SEVEN PLUS 200 mg/5 ml ORAL SUSPENSION

IBUPROFEN 200 MG/5 ML ORAL SUSPENSION

PL 04917/0099 AND 0121

### STEPS TAKEN FOR ASSESSMENT

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the Marketing Authorisation application on 8\textsuperscript{th} March 2010.</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 16\textsuperscript{th} March 2010.</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the applications, the MHRA requested further information on the quality section of the dossier on 6\textsuperscript{th} September 2011.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on the quality section of the dossier on 17\textsuperscript{th} October 2011.</td>
</tr>
<tr>
<td>5</td>
<td>The application was approved on 20\textsuperscript{th} October 2011.</td>
</tr>
</tbody>
</table>
IBUPROFEN SEVEN PLUS 200 mg/5 ml ORAL SUSPENSION

IBUPROFEN 200 MG/5 ML ORAL SUSPENSION

PL 04917/0099 AND 0121

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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</table>
1. **NAME OF THE MEDICINAL PRODUCT**

Ibuprofen Seven Plus 200 mg/5 ml 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: 5ml up to three times in 24 hours
- 10 to 12 years: 7.5ml up to three times in 24 hours

If the child’s symptoms persist for more than three days, consult a doctor.
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.

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 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)

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. ≤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.

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.

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.

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 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 75 mg
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.

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.

4.7 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, melena, 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 aspetic 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 trial and epidemiological data suggest that use of ibuprofen (particularly at high doses 2400 mg daily) and in long-term treatment 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.

### 4.9 Overdose

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

**Symptoms**

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

**Management**

Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

### 5.1 Pharmacodynamic properties
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 if ibuprofen 400mg was taken within eight hours before or within 30 minutes after immediate release aspirin dosing (81mg), a decreases effect of aspirin on the formation of thromboxane or platelet aggregation occurred. However, the limitation 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 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 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
20/10/2011

10 DATE OF REVISION OF THE TEXT
02/02/2017
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Ibuprofen 200 mg/5 ml 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 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
Children under 12 years
Rheumatic or muscular pain, headache, dental pain, feverishness (including post-immunisation pyrexia), symptoms of cold and influenza.

Over 12 years
Rheumatic or muscular pain, pain of non-serious arthritic conditions, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness, symptoms of colds and influenza.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
For oral administration and short-term use only.
Leave at least four hours between doses and do not take more than the recommended amount in any 24 hour period.
Not to be given to children under 3 months of age, except on the advice of a doctor.
This product should only be given to infants who weigh more than 5kg.

If the child’s (aged over 6 months) symptoms persist for more than 3 days, consult your doctor promptly. For children aged 3 to 6 months, medical advice should be sought promptly after 24 hours symptoms persist.

The daily dosage for children is 20-30mg/kg bodyweight in divided doses. Using the dosing device provided this can be achieved as follows:
3 to 6 months (weighing more than 5 kg): 1.25ml (50mg), up to 3 times in 24 hours.
6 to 12 months (weighing 8-10 kg): 1.25ml (50mg), up to 3 to 4 times in 24 hours.
1 to 4 years (weighing 10-15 kg): 2.5ml (100mg), up to 3 times in 24 hours.
4 to 7 years (weighing 15-20 kg): 3.75ml (150mg), up to 3 times in 24 hours.
7 to 12 years (weighing 20-40 kg): 5 ml (200mg), up to 3 times in 24 hours.
Over 12 years: 5 ml (200mg) to 10ml (400mg) up to three times in 24 hours (maximum daily dose 1200mg)

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

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

Children over 6 months to 12 years should not take Ibuprofen 200mg/5ml Oral Suspension for longer than 3 days unless your doctor tells you to.

Those aged 12 years or over should not take Ibuprofen 200mg/5ml Oral Suspension for longer 10 days unless your doctor tells you to.

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

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

If symptoms persist or worsen consult your doctor.

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

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

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

Last trimester of pregnancy (see section 4.6).

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

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

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

Suspected haemopoietic disorder.

Cerebrovascular or other active bleeding.

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

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration necessary to control symptoms (see section 4.2 GI and cardiovascular risks below)

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

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

Other NSAIDs:
The use of Ibuprofen 200 mg/5 ml Oral Suspension with concomitant NSAIDs including cylooxygenase-2 selective inhibitors should be avoided (see section 4.5)

SLE and mixed connective tissue disease:
Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8).

Asthmatic patients are to seek their doctor’s advice before using ibuprofen (see below)

Renal:
Renal impairment as renal function may further deteriorate (see sections 4.3 and 4.8)
Administration of NSAIDs such as Ibuprofen may cause dose dependent renal toxicity in patients with reduced renal blood flow or blood volume where renal prostaglandins support the maintenance of renal perfusion. Patients at risk of this reaction include those with impaired renal function, heart failure or liver dysfunction. This is of
UKPAR Ibuprofen Seven Plus/Ibuprofen 200 mg/5ml Oral Suspension  PL 04917/0099 and 0121

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.

**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 trial and epidemiological data suggest that use of ibuprofen, particularly at high doses (2400mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200mg daily) is associated with an increased risk of myocardial infarction.

**Respiratory:**
Ibuprofen should be used with caution in patients with bronchial asthma or allergic disease, since such patients may have NSAID – sensitive asthma which has been associated with severe bronchospasm.

**Gastrointestinal:**
NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn’s disease) as these conditions may be exacerbated (see section 4.8).

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events.

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available.

Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low-dose acetysalicylic acid, or other medicinal products likely to increase gastrointestinal risk (see below and section 4.5).

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin (see section 4.5).

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

**Skin reactions:**
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens- Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8).

Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Ibuprofen 200mg/5ml Oral Suspension should be discontinued at the first appearance of skin rash, mucosal lesion, or any other sign of hypersensitivity. Exceptionally, varicella can be at the origin of serious cutaneous and soft tissues infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of Ibuprofen Oral Suspension in case of varicella (Chicken pox).

During the prolonged use of analgesics headaches may occur which must should not be treated with elevated doses of the medicinal product. In general the habitual intake of analgesics, particularly the combination use of different analgesic substances, may cause permanent renal damage and a risk of renal failure (analgesics nephropathy). This risk may be increased under physical strain associated with loss of salt and dehydration therefore it should be avoided.
Ibuprofen may temporarily inhibit the blood platelet function (thrombocyte aggregation) and prolong the bleeding time. Patients with coagulation defects or on anticoagulant therapy should be observed carefully.

In case of prolonged treatment with ibuprofen a periodical monitoring of hepatic and renal function as well as the blood count is necessary, especially in high risk patients.

Consumption of alcohol should be avoided since it may intensify side effects of NSAIDs, especially if affecting the gastrointestinal tract or the central nervous system.

Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed very rarely. At the first signs of a hypersensitivity reaction after taking/administering Ibuprofen, therapy must be stopped. Medically required measures, in line with the symptoms, must be initiated by specialist personnel.

Caution is required in the following patients:
- patients with congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria)
- patients who are dehydrated
- patients directly after major surgical procedures

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

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Ibuprofen should be avoided in combination with:

Aspirin: Unless low-dose aspirin (not above 75 mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (see section 4.4).

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: as a result of synergistic effects, avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects (see section 4.4). Co-administration of ibuprofen with other NSAIDs should therefore be avoided (see section 4.4).

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

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

Ibuprofen should be used with caution in combination with:

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

Diuretics, ACE inhibitors, beta-receptor blocking medicines and angiotensin-II antagonists: NSAIDs may reduce the effect of diuretics and other antihypertensive drugs. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor, beta-receptor blocking medicines or angiotensin-II antagonists and agents that inhibit cyclooxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

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

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

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

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

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

Ciclosporin: Increased risk of nephrotoxicity.

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

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

Methotrexate: There is potential of an increase in plasma methotrexate.

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

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

Ritonavir: May increase the plasma concentrations of NSAIDs.

Moclobemide: Enhances the effect of ibuprofen.

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

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

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

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

Baclofen: Elevated baclofen toxicity.

4.6 FERTILITY, PREGNANCY AND LACTATION

Pregnancy
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastrochisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1 %, up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-fetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

During the first and second trimesters of pregnancy, ibuprofen should not be given unless clearly necessary. If ibuprofen is used by a woman attempting to conceive, or during the first and second trimesters of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the fetus to:
- Cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- Renal dysfunction, which may progress to renal failure with oligo-hydroamniosis;
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.

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

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

### 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

None expected at recommended dose and duration of therapy

### 4.8 UNDESIRABLE EFFECTS

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

- **Very common:** \( \geq 1/10 \)
- **Common:** \( \geq 1/100 \) to \( < 1/10 \)
- **Uncommon:** \( \geq 1/1000 \) to \( < 1/100 \)
- **Rare:** \( \geq 1/10,000 \) to \( < 1/1000 \)
- **Very rare:** \(< 1/10,000 \)
- **Not known:** cannot be estimated from the available data

With the following adverse drug reactions, it must be accounted for that they are predominantly dose-dependent and vary interindividually.

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melena, haematemeses, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following administration. Less frequently, gastritis has been observed.

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

Clinical trial and epidemiological data suggest that use of ibuprofen (particularly at high doses 2400mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

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

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

**Infections and infestations:**

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

If signs of an infection occur or get worse during use of this product, the patient is therefore recommended to go to a doctor without delay. It is to be investigated whether there is an indication for an anti-infective/antibiotic therapy.
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Very rare: the symptoms of aseptic meningitis with neck stiffness, headache, nausea, vomiting, fever or consciousnesses clouding have been observed under ibuprofen. Patients with autoimmune disorders (SLE, mixed connective-tissue disease) appear to be predisposed.

**Blood and lymphatic system disorders:**
Very rare: Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, and agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising. In such cases, the patient should be advised to discontinue the medicine immediately, to avoid any self-medication with analgesics or antipyretics and to consult a physician.

The blood count should be checked regularly in long-term therapy

**Immune system disorders:**
Uncommon: Hypersensitivity reactions with skin rash and pruritis, as well as asthma attacks (possibly with drop in blood pressure).

The patient is to be instructed to inform a doctor at once and no longer to take Ibuprofen in this case.

Very rare: Severe general hypersensitivity reactions.

They may present as facial oedema, swelling of the tongue, swelling of the internal larynx with constriction of the airways, respiratory distress, racing heart, drop in blood pressure up to life-threatening shock.

If one of these symptoms occurs, which can happen even on first use, the immediate assistance of a doctor is required.

**Psychiatric disorders:**
Very rare: psychotic reactions, depression

**Nervous system disorders:**
Uncommon: central nervous disturbances such as headache, dizziness, sleeplessness, agitation, irritability or tiredness.

**Eye disorders:**
Uncommon: visual disturbances.

**Ear and labyrinth disorders:**
Rare: tinnitus.

**Cardiac disorders**
Very rare: palpitations, heart failure, myocardial infarction.

**Vascular disorders:**
Very rare: arterial hypertension.

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

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

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

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

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

**Skin and subcutaneous tissue disorders:**
Uncommon: Various skin rashes, photosentivity

Very rare: Severe forms of skin reactions such as bullous reactions, including Stevens
In exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection (see also "Infections and infestations").

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

Very rare: reduced urinary excretion and formation of oedemas, particularly in patients with arterial hypertension or renal insufficiency, nephrotic syndrome, interstitial nephritis that may be accompanied by acute renal insufficiency.

Renal function should therefore be checked regularly.

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

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

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

Management
Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma

5 PHARMACOLOGICAL PROPERTIES
5.1 PHARMACODYNAMIC PROPERTIES
Pharmacotherapeutic group: anti-inflammatory and antirheumatic products, non steroids; propionic acid derivatives

ATC Code: M01 AE01

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) that in the conventional animal-experiment inflammation models has demonstrated its efficacy by inhibition of prostaglandin synthesis. In humans, ibuprofen reduces inflammatory pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits ADP – and collagen-induced 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 if ibuprofen 400mg was taken within 8 hours before or within 30 minutes after immediate release aspirin dosing (81mg), a decreases effect of aspirin on the formation of thromboxane or platelet aggregation occurred. However, the limitation 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 is considered to be likely for occasional ibuprofen use.

5.2 PHARMACOKINETIC PROPERTIES
Absorption
UKPAR Ibuprofen Seven Plus/Ibuprofen 200 mg/5ml Oral Suspension

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

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

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

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

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

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

Furthermore no carcinogenic effects have been observed in mice and rats.
Ibuprofen inhibits ovulation in rabbits and impairs implantation in various animal species (rabbit, rat, and mouse). In reprotoxicity studies in rats and rabbits; ibuprofen crossed the placenta. At dose causing toxicity to the mother, malformations (ventricular septal defects) occurred more frequently in the progeny of rats.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS
Glycerol
Xanthan gum,
Liquid Maltitol,
Polysorbate 80,
Saccharin sodium,
Citric acid monohydrate (for pH ajustment),
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 25ºC. Store in the original pack.

6.5 NATURE AND CONTENTS OF CONTAINER
An amber glass bottle sealed with child resistant, tamper evident cap.
Pack sizes available: 60 ml, 80ml, 100 ml, 150 ml and 200 ml.
Not all pack sizes may be marketed.
A double ended spoon with measures of 1.25ml 2.5ml or 5ml is provided.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
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),
Ballymacarbery,
UKPAR Ibuprofen Seven Plus/Ibuprofen 200 mg/5ml Oral Suspension
Clonmel,
Co. Tipperary, Ireland.

8 MARKETING AUTHORISATION NUMBER(S)
   PL 04917/0099
   PL 04917/0121

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
   20/10/2011

10 DATE OF REVISION OF THE TEXT
    01/11/2011
Package leaflet: Information for the user
Ibuprofen Seven Plus 200 mg/5 ml 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 Seven Plus 200 mg/5 ml 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 the 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. In case of side effects
5. How to store Ibuprofen Seven Plus
6. Contents of the pack and further 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 paracetamol, 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 should not be used for more than 3 days.

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 an allergy reaction such as wheezing, an asthma attack, runny nose, skin reaction or swelling after taking aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs)
- has ever had a stomach bleed 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 70 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 7 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:
- 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
-containing medicines (used in the treatment of heart problems, such as digoxin)
-ciclosporin or sirolimus (used to suppress the body’s immune system)
-corticosteroids (anti-inflammatory drugs, such as prednisolone or beclometasone)
- diuretics (to help pass water such as furosemide or bendrofluazide)
- lithium, or selective serotonin reuptake inhibitors (SSRIs - such as fluoxetine) used to treat mood disorders
- methotrexate (used to treat psoriatic arthritis, psoriasis and some cancers)
- nitrates (used to terminate pregnancy)
- oral contraceptives (used to treat a wide range of infections e.g. gonorrhoea)
- oestrogen (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:
- salbutamol (EFS) may have a mild laxative effect (calorific value 2.3 kcal). If you have been told that you or your child has an intolerance to some sugars, contact your doctor before taking/giving this medicine.

The following warnings are less likely to apply to children but should be considered before giving this medicine:
- 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, talk to 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 last 3 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 concentrations 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.
UKPAR Ibuprofen Seven Plus/Ibuprofen 200 mg/5ml Oral Suspension

PKL 04917/0099 and 0121

- If you have a family history of heart disease or stroke, or if you are a smoker.

Driving and using machines

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

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 pharmacist if you are unsure. See the section 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

Do not give to children under 7 years of age, or of those weighing less than 20 kg.

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 blisters or peeling of the skin), itching or swelling, light-headedness, rash of the heat fluid retention e.g. swollen ankles, not passing enough water
- stiff neck, headache, nausea, vomiting, tinnitus 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 urea levels.

Very Rare:

- occasionally hypersensitivity reactions may occur which can cause skin rashess as well as asthma attacks, swelling of the tongue and breathinglessness
- liver problems may occur with ibuprofen
- passing less urine than normal, increased proteins in the blood (detected by test)
- order’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 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:

Ei 5ml contains 100mg of the active ingredient ibuprofen. The other ingredients are: glycolal (E422), sucrose, gum, methylcellulose (E946), polyethylene 80, sorbitol, sodium citrate, sodium benzoate, 221, magnesium aluminium silicate, purified water and strawberry flavour (contains propylene glycol).

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

Ibuprofen Seven Plus is a colourless, white oral suspension. This medicine comes in amber glass bottles containing 50 ml, 80 ml or 100 ml with a child-resistant closure. Not all pack sizes may be marketed. A double ended spoon with measure 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:

Pine Wood Laboratories Ltd., Ballymacarthy, Clonmel Co.
Tipperary, Ireland.

Manufacturers:

Pine Wood Laboratories Ltd., Ballymacarthy, Clonmel Co.
Tipperary, Ireland.
PL Number: 04917/0099

Other sources of information:

- To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge, 0800 198 560 (UK only). Please be ready to give the following information: Product name: Ibuprofen Seven Plus 200mg/5ml Oral Suspension. Reference number: PL/04917/0099

This is a service provided by the Royal National Institute of Blind People.

This leaflet was last updated in September 2016 26/09/1415PM

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UKPAR Ibuprofen Seven Plus/Ibuprofen 200 mg/5ml Oral Suspension

PL 04917/0099 and 0121

PACKAGE LEAFLET: INFORMATION FOR THE USER
Ibuprofen 200 mg/5 ml Oral Suspension

Read all of this leaflet carefully before you start taking/giving this medicine.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if symptoms persist or worsen after 1 day (infants aged 3-6 months) or 3 days (children aged 6 months to 12 years) or 10 days (for those aged over 12 years).
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Ibuprofen 200 mg/5 ml Oral Suspension is and what it is used for
2. Before you give/take Ibuprofen 200 mg/5 ml Oral Suspension
3. How to give/take Ibuprofen 200 mg/5 ml Oral Suspension
4. Possible side effects
5. How to store Ibuprofen 200 mg/5 ml Oral Suspension
6. Further Information

1. WHAT IBUPROFEN 200 MG/5 ML ORAL SUSPENSION IS AND WHAT IT IS USED FOR
Ibuprofen 200 mg/5 ml Oral Suspension contains Ibuprofen as the active ingredient. This belongs to a group of medicines called non-steroidal anti-inflammatory agents. This effect is reversible so stopping the use of the drug may relieve the symptoms. It is unlikely that Ibuprofen is used occasionally, will affect your chances of becoming pregnant, however, tell your doctor before taking this medicine if you have problems becoming pregnant.

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

Medicines such as Ibuprofen 200 mg/5 ml Oral Suspension 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. If you have heart problems, previous stroke or if you think that you or your child might be at risk of these conditions (for example if you or your child have high blood pressure, diabetes, high cholesterol or are a smoker) you should discuss the treatment with your doctor or pharmacist.

Drinking alcohol while taking Ibuprofen may increase your risk of certain side effects.

2. BEFORE YOU GIVE/TAKE IBUPROFEN 200 MG/5 ML ORAL SUSPENSION
Do not give/take this medicine if you or 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 or wheezing e.g. 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)
- has ever had severe kidney, heart or liver problems
- is suffering from severe dehydration
- has an inherited intolerance to some sugars
- is less than 3 months old, except on the advice of a doctor
- suffers from a blood disorder
- are in the last three months of pregnancy
- are trying to conceive.

Take special care and check with your doctor or pharmacist before taking this medicine if you are elderly or your child suffers from:
- high blood pressure, heart problems or a stroke because there is a small increased risk of heart problems and stroke with Ibuprofen
- kidney, liver or bowel problems
- lupus (SLE) or a mixed connective tissue disease
- a chronic inflammatory bowel disease such as ulcerative colitis or Crohn’s disease
- asthma or allergic diseases of the lungs
- has chicken-pox
- has a disorder of porphyrin metabolism.

Speak to your doctor or pharmacist before taking if you are trying to get pregnant. Ibuprofen belongs to a group of medicines which may impair fertility in women. This effect is reversible so stopping the use of the drug may relieve the symptoms. It is unlikely that Ibuprofen is used occasionally, will affect your chances of becoming pregnant, however, tell your doctor before taking this medicine if you have problems becoming pregnant.

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

Drinking alcohol while taking Ibuprofen may increase your risk of certain side effects.

Taking other medicines
Please tell your doctor or pharmacist if you or your child is taking or has recently taken any other medicines, including medicines obtained without a prescription. In particular, tell your doctor if you or your child are taking any of the following:
- Low-dose aspirin (up to 75 mg a day)
- Diuretics (drugs to help you pass water)
- Anti-coagulants e.g. Warfarin and Heparin and Anti-platelet drugs such as Clopidogrel and Ticlopidine (drugs that thin the blood)
- Antihypertensives (drugs used to treat high blood pressure e.g. Captopril or Propranolol)
- Lithium, Phenytoin or Selective serotonin reuptake inhibitors (SSRI’s e.g. Fluoxetine used to treat mood disorders)
- Methotrexate (used to treat rheumatoid arthritis, psoriasis and some cancers)
- Zidovudine (used to treat HIV)
- Corticosteroids (anti-inflammatory drugs, such as prednisone)
- Cardiac glycosides (drugs used in the treatment of heart problems, such as Digoxin)
- Opioid or Trazodone (used to suppress the body’s immune system)
- Quinolone antibiotics (used to treat a wide range of infections e.g. Ciprofloxacin)
- Probencid and sulfinpyrazone (used to treat gout)
- Moobidiemide (used to treat depression)
- Aminoglycosides (an antibiotic)
- Cholesteryamine (used to reduce cholesterol)
- Baclofen (used to relax muscles)
- Sulphonylureas (used to treat diabetes)
- Ritonavir (used to treat HIV infection and AIDS)
- Bisphosphonates (used to prevent loss of bone mass)
- Oxyphenylamine (used to treat poor circulation to arms and legs)
- any other Ibuprofen preparations or NSAID painkillers, including those you can buy without a prescription.

If you are not sure about any of the medicines your child is taking, ask your pharmacist for advice.

Pregnancy and breast-feeding
Ibuprofen should NOT be taken during the last 3 months of pregnancy, as it may be harmful to the unborn child. Pregnant women intending to use this product should seek medical advice before use as it should only be taken on doctor’s advice during the first 6 months of pregnancy.

Only small amounts of Ibuprofen and its breakdown products pass into breast milk. As no harmful effects to infants are known to date, it is not usually necessary to stop breast-feeding during short-term use of ibuprofen at the recommended doses.
UKPAR Ibuprofen Seven Plus/Ibuprofen 200 mg/5ml Oral Suspension

PL 04917/0099 and 0121

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

3. HOW TO GIVE/TAKE IBUPROFEN 200 MG/5 ML ORAL SUSPENSION

Shake the bottle well before measuring the dose. A measuring device is provided to ensure accuracy. Contact your doctor for advice if symptoms persist or worsen for more than 10 days in those aged over 12 years. For children aged 6 months to 12 years contact a doctor if symptoms persist or worsen after 3 days. For infants aged 3 months to 6 months contact a doctor if symptoms persist or worsen after 24 hours.

This medicine should NOT be given if your child weighs less than 5 kg. The usual daily dose in children is 20 - 30 mg per kg of bodyweight in divided doses. Leave at least 4 hours between doses. For oral and short term use only.

<table>
<thead>
<tr>
<th>Babies under 3 months</th>
<th>Do not give except on the advice of a doctor</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 - 6 months (weighing more than 5 kg)</td>
<td>1.25 ml dose (50 mg) taken up to 3 times in 24 hours</td>
</tr>
<tr>
<td>6 - 12 months (weighing 6 - 10 kg)</td>
<td>1.25 ml dose (50 mg) taken up to 3 times in 24 hours</td>
</tr>
<tr>
<td>1 - 4 years (weighing 10 - 15 kg)</td>
<td>2.5 ml dose (100 mg) taken up to 3 to 4 times in 24 hours</td>
</tr>
<tr>
<td>4 - 7 years (weighing 15 - 20 kg)</td>
<td>3.75 ml dose (150 mg) taken up to 3 times in 24 hours</td>
</tr>
<tr>
<td>7 - 12 years (weighing 20 - 40 kg)</td>
<td>5 ml dose (200 mg) taken up to 3 times in 24 hours</td>
</tr>
<tr>
<td>Over 12 years</td>
<td>5 ml to 10 ml dose (200 mg - 400 mg) taken 3 times in 24 hours. Do not give more than 30 ml (1200 mg) in any 24 hours.</td>
</tr>
</tbody>
</table>

Post-immunisation fever: One 1.25 ml, followed by another 1.25 ml six hours later if necessary. Not more than 2 doses should be given in 24 hours. If fever is not reduced, consult a doctor.

If you forget to give/take this medicine
If you forget to give/take a dose, give/take it as soon as you remember, unless it is almost time for the next dose. Never give a double dose to make up for the missed dose.

If you give/take more medicine than you should
If you or your child takes a lot 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.

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/taking 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, tightness in chest, swelling 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/taking the medicine and tell your doctor:
- If you or your child’s skin starts to turn red or they develop a varied skin reaction or their skin starts to blister or peel, this is very rare
- Unexplained stomach pain, indigestion, heartburn, feeling sick and/or vomiting
- Yawning 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.
  - Ibuprofen 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
  - Depression or psychotic reactions
  - Hair loss
  - High blood pressure.

If any of these side effects gets worse, or if you notice a side effect not listed in this leaflet, tell your doctor or pharmacist.

5. HOW TO STORE IBUPROFEN 200 MG/5 ML ORAL SUSPENSION
Keep out of the reach and sight of children. Do not use after the expiry date shown on the bottle, the expiry date refers to the last day of that month. Do not store above 25°C. Medicines should not be disposed of via wastewater, ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION
What ibuprofen 200 mg/5 ml Oral Suspension contains
The active ingredient is Ibuprofen 200 mg per 5 ml.
The other ingredients are: Glycerol (E422), Xanthan Gum, 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 200 mg/5 ml Oral Suspension looks like and contents of the pack
Ibuprofen 200 mg/5 ml Oral Suspension is a colour-free, white oral suspension. This medicine comes in amber glass bottles containing: 60 ml, 80 ml, 100 ml, 150 ml or 200 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 3 months of first opening.

Marketing Authorisation Holder
Pinewood Laboratories Ltd., Ballymacarbry, Cloneel, Co. Tipperary, Ireland.

Manufacturer
Pinewood Laboratories Ltd., Ballymacarbry, Cloneel, Co. Tipperary, Ireland.

PL Number: 04917/0121
This leaflet was last approved in September 2011
Ibuprofen Seven Plus 200 mg/5 ml Oral Suspension

Read the package leaflet before use.

Ibuprofen Seven Plus is a strawberry flavoured ibuprofen suspension for children aged 7 to 12 years. It is intended for short-term use for the relief of rheumatic, muscular pain, headache, dental pain, toothache and symptoms of colds and influenza. Do not give to children under 7 years.

Ingredients:
Each 5 ml of oral suspension contains 200 mg ibuprofen. Also contains: liquid maltitol (E965) and sodium tartrazine. See labelling for further information.

Keep out of the sight and reach of children.

Storage:
- Do not store above 25°C
- Store in the original packaging
- Discard 3 months after opening.

Dosage:
For children aged 7 to 12 years
- Do not give this product if your child:
  - Has, or has had, blood or stomach bleeding
  - Has had an allergic reaction to ibuprofen or any other ingredients of the product, aspirin or other nonsteroidal anti-inflammatory drugs
  - Is taking other NSAID painkillers, or aspirin with a dose above 7.5 mg/kg
  - Is planning to have a surgical operation or before giving any immunisation, if your child
- Follow the recommended dosage for your child's age group.
- If symptoms persist or worsen, consult your doctor.

Always use Ibuprofen Seven Plus exactly as indicated. Check with your doctor or pharmacist if you are unsure.

For oral use:
Shake the bottle well before use.

DOSAGE: Use the measuring device provided.

<table>
<thead>
<tr>
<th>Age</th>
<th>How much (up to 3 doses in 24 hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 7 years</td>
<td>One 5 ml suspension</td>
</tr>
<tr>
<td>7 - 9 years</td>
<td>One 5 ml suspension</td>
</tr>
<tr>
<td>10 - 12 years</td>
<td>One 5 ml suspension and one 3.5 ml suspension</td>
</tr>
</tbody>
</table>

Do not give more medicine than the label tells you to.

Do not give:
- to children under 7 years of age, or those weighing less than 30 kg
- more than 3 doses in any 24-hour period
- Separately every 8-12 hours. Leave at least 4 hours between doses
- for more than 3 days

UKPAR Ibuprofen Seven Plus/Ibuprofen 200 mg/5ml Oral Suspension
PL 04917/0099 and 0121
Ibuprofen Seven Plus 200 mg/5 ml Oral Suspension

Double Strength

For children aged 7 to 12 years

Read the package leaflet before use.

Ibuprofen Seven Plus is a strawberry flavoured ibuprofen suspension for children aged 7 to 12 years. It is intended for short term use for the relief of rheumatic or muscular pain, headache, dental pain, teething pain and symptoms of colds and influenza. Do not give to children under 7 years.

Ingredients:
Each 5 ml of oral suspension contains 200 mg ibuprofen. Also contains: liquid maltitol (E965) and sodium benzoate. See leaflet for further information.

Keep out of the sight and reach of children.

Storage:
• Do not store above 25°C
• Store in the original package
• Discard 3 months after opening

For children aged 7 to 12 years

Do not give this product if your child:
• Has, or has ever had two or more episodes of stomach ulcers
• Has peptic ulcer disease
• Has had a reaction to ibuprofen or any other components of this product
• Is taking any other painkillers or aspirin with a daily dose above 75 mg
• Speaks to a pharmacist or doctor before giving the product to your child

In children, if symptoms persist or worsen, consult your doctor.

Always use Ibuprofen Seven Plus exactly as indicated. Check with your doctor or pharmacist if you are unsure.

For oral use:
Do not use the bottle seal to open.

Dosage:
Use the measuring device provided.

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

Do not give more medicine than the label tells you to.

Do not give:
• to children under 7 years of age or
• to those weighing less than 20 kg
• more than 3 doses in any 24 hour period
• Separate the doses evenly (every 6-8 hours). Leave at least 4 hours between doses
• for more than 3 days.
UKPAR Ibuprofen Seven Plus/Ibuprofen 200 mg/5ml Oral Suspension

PL 04917/0099 and 0121

Effective relief from aches, pain and fever in children from
seven to twelve years.
Do not use for children under 7 years or those who weigh
less than 20 kg.
Each 5 ml of oral suspension contains 200 mg ibuprofen.
Also contains: E966 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 cholesel,
high blood pressure, a stroke, heart, liver, kidney or
bowel problems.

Children from 7 to 12 years

Ibuprofen

SEVEN PLUS

200 mg/5 ml

ORAL SUSPENSION

Double Strength

Sugar & colour free

Strawberry flavour

100 ml

For short term use only.
If symptoms persist or worsen,
consult your doctor.
Do not store above 25°C.

PL Holder: Pinewood Laboratories
Ltd, Ballymacarthy, Clonmel, Co.
Tipperary, Ireland.
PL: 04917/0099 23LL

D/N: EXP:

Each 5 ml of the oral suspension contains 200 mg of the
active ibuprofen. Also Includes Matilho (E966) and Sodium
Benzoate (E211). See leaflet for further information.

For oral use.
Keep out of the reach and sight of children.
This medicine should be used within 3 months of first opening.

WARNING: DO NOT EXCEED THE STATED DOSE

Marketing Authorisation Holder:
Pinewood Laboratories Ltd.,
Ballymacarthy, Clonmel,
Co. Tipperary, Ireland.
PL Number: 04917/0121
23LL

POM
Each 5 ml of the oral suspension contains 200 mg of the active ibuprofen. Also includes Maltitol (E965) and Sodium Benzoate (E211). See leaflet for further information.
For oral use.
Keep out of the reach and sight of children.
This medicine should be used within 3 months of first opening.

WARNING: DO NOT EXCEED THE STATED DOSE

PL Number: 049/170121
23LL

Ibuprofen
200 mg/5 ml
Oral Suspension

Each 5 ml of the oral suspension contains 200 mg of the active ibuprofen. Also includes Maltitol (E965) and Sodium Benzoate (E211). See leaflet for further information.
For oral use.
Keep out of the reach and sight of children.
This medicine should be used within 3 months of first opening.

WARNING: DO NOT EXCEED THE STATED DOSE

Shake the bottle well before use.
Please use measuring device provided.

DOSAGE: CHILDREN (weighing over 5 kg)
3 - 4 years: (weighing under 10 kg) 1.25 ml once 12.5 mg taken up to 3 times in 24 hours
1.625 ml taken up to 3 times in 24 hours
6 - 10 years: (weighing 10 - 19 kg) 2.5 ml four times 25 mg taken up to 3 times in 24 hours
5 ml four times in 24 hours
11 - 12 years: (weighing 10 - 20 kg) 3.75 mg four times 37.5 mg taken up to 3 times in 24 hours
Over 12 years: 5 ml taken up to 3 times in 24 hours

Do not give to babies under 3 months, except on the advice of a doctor.
Post-infection fever: 1.25 ml followed by another 1.25 ml six hours later if necessary. Not more than 2 doses should be given in 24 hours. If fever is not reduced, consult a doctor.

Ibuprofen
200 mg/5 ml
Oral Suspension

PL Number: 049/170121
23PC

60ml die
47x47x102

IBUPROFEN 200 MG/5 ML
ORAL SUSPENSION
Please note the below reclassification only applies to Ibuprofen Seven Plus 200mg/5ml Oral Suspension (PL 04917/0099).

Annex 1

Public Assessment Report

Prescription only medicine to Pharmacy Reclassification

Ibuprofen Seven Plus 200mg/5ml Oral Suspension

PL 04917/0099

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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.

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

The Commission on Human Medicines has advised that this product can be available as a Pharmacy medicine. This report outlines the evidence that the MHRA reviewed which led to the decision to approve this application.

What is in Ibuprofen Seven Plus?

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

This is the first product containing liquid ibuprofen product at 200mg/5ml strength to be available without prescription. Only one strength of liquid ibuprofen has previously 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. |

Who has made the proposal?

The licence-holder for Ibuprofen Seven Plus (Pinewood Laboratories Limited) 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.

3. Proposed terms of reclassification

What are the details of this change?
Ibuprofen Seven Plus will be made available through Pharmacy outlets under the following conditions:

- 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 the proposal was assessed

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. A direct healthcare professional communication (DHPC) will be sent to pharmacists as a risk minimisation measure.

6. Consultation on Pharmacy availability
Consultation document ARM 91, which summarises the proposals on the proposal to make Ibuprofen Seven Plus available from pharmacies was posted on the gov.uk website on 15 March 2016. The deadline for comments was 4 April 2016. ARM 91 can be accessed via the following link:

Five responses were received.
Four responses agreed with the proposal, and one respondent was not sure about the proposal.

Of these five responses received, three of these were from specified organisations: Dispensing Doctors’ Association; Royal Pharmaceutical Society; Guild of Healthcare Pharmacists. One response was from a Pharmacist/Regulatory Affairs Consultant, and one was from a lay person with an interest in pharmacy.

Overall, no new issues of concern have been raised in relation to Pharmacy availability of Ibuprofen Seven Plus as the responses reflected concerns about the readability and layout of the product information. The patient information leaflet text and design have been revised, improved and user-tested to ensure that patients can make an informed decision about this medicine.

7. Conclusion

Assessment of the responses to consultation on the application for Ibuprofen Seven Plus has revealed no new issues of concern in addition to those already considered by CHM and on which CHM were reassured. In light of the advice from the Commission on Human Medicines the Licensing Authority has taken the decision to approve Pharmacy legal status for Ibuprofen Seven Plus.