Public Assessment Report

Ibuprofen 100 mg/5ml oral suspension

(Ibuprofen)

UK Licence No.: PL 00037/0677

Abbott Laboratories Limited
Lay Summary
Ibuprofen 100 mg/5ml oral suspension
(Ibuprofen)

This is a summary of the Public Assessment Report (PAR) for Ibuprofen 100 mg/5ml oral suspension (PL 00037/0677). This medicinal product will be referred to as Ibuprofen oral suspension in this lay summary for ease of reading.

This summary explains how Ibuprofen oral suspension was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use Ibuprofen oral suspension.

For practical information about using Ibuprofen oral suspension, patients should read the package leaflet or contact their doctor or pharmacist.

What is Ibuprofen oral suspension and what is it used for?
This medicine is the same as Brufen Syrup (PL 46302/0011; Mylan Products Limited), which is already authorised in the UK. The licence holder (Mylan Products Limited) for Brufen Syrup (PL 46302/0011) has agreed that its own scientific data can be used as a basis for the grant of an identical licence for Ibuprofen oral suspension (PL 00037/0677).

Ibuprofen oral suspension can be used to relieve pain and inflammation in conditions such as osteoarthritis, rheumatoid arthritis (including juvenile rheumatoid arthritis or Still’s disease), arthritis of the spine, ankylosing spondylitis, swollen joints, frozen shoulder, bursitis, tendinitis, tenosynovitis, lower back pain, sprains and strains.

Ibuprofen oral suspension can also be used to treat other painful conditions such as toothache, pain after operations, period pain and headache, including migraine. In addition, Ibuprofen oral suspension can be used for the short-term treatment of fever in children over the age of 1 year.

How does Ibuprofen oral suspension work?
Ibuprofen oral suspension contains the active ingredient ibuprofen which belongs to a group of medicines called anti-inflammatory pain killers. This medicine helps relieve pain.

How is Ibuprofen oral suspension used?
Ibuprofen oral suspension is taken by mouth, preferably with or after food. The bottle should be shaken well before use.

Patients must take this medicine exactly as a doctor has told them. If they are not sure they should refer to instructions on the carton or check with their doctor or pharmacist.

The usual dosage in adults and children over 12 years is 4 to 6 spoonfuls (5 ml) taken three times a day. A doctor may choose to increase or decrease this depending on what a patient is being treated for; but no more than 24 spoonfuls (120 ml/2400 mg) should be taken in one day.
Ibuprofen should NOT be taken by children weighing less than 7 kg. When used to treat fever, the suspension should not be used long term or given to children under the age of 1 year. The usual dose in children is 20 mg per kg of bodyweight each day, in divided doses. This can be given as follows:

- 1-2 years: One 2.5 ml (50 mg) dose three/four times a day
- 3-7 years: One 5 ml (100 mg) dose three/four times a day
- 8-12 years: Two 5 ml (200 mg) doses three/four times a day

The doctor may choose to increase this dose in children with juvenile rheumatoid arthritis. This dose should not exceed 40mg/kg bodyweight daily in divided doses. A patient should avoid excessive use of painkillers. If a patient usually takes painkillers, especially combinations of different painkillers, he/she may damage their kidneys. A patient must tell a doctor if he/she is already taking another painkiller before taking this medicine and a doctor will decide whether they should take this medicine. This risk may be increased if a patient is dehydrated.

Please read section 3 of the package leaflet for detailed information on dosing recommendations, the route of administration, and the duration of treatment.

Ibuprofen oral suspension can only be obtained with a prescription from a doctor.

**What benefits of Ibuprofen oral suspension has been shown in studies?**
The application for Ibuprofen oral suspension (PL 00037/0677) is considered to be identical to the previously authorised licence for Brufen Syrup (PL 46302/0011), with the same benefits and risks. So, no new studies have been provided for Ibuprofen oral suspension (PL 00037/0677). However, reference is made to the studies for Brufen Syrup (PL 46302/0011).

**What are the possible side effects of Ibuprofen oral suspension?**
Like all medicines, Ibuprofen oral suspension can cause side effects, although not everybody gets them.

The common side effects with Ibuprofen oral suspension (which may affect up to 1 in 10 people) are rash, feeling dizzy or tired, stomach pain, indigestion, diarrhoea, feeling sick, being sick, wind, constipation, headache (if this happens while a patient is taking this medicine it is important not to take any other medicines for pain to help with this), passing black tarry stools, passing blood in the faeces (stools/motions) and vomiting any blood.

For the full list of all side effects reported with Ibuprofen oral suspension, see section 4 of the package leaflet.

For the full list of restrictions, see the package leaflet.

**Why was Ibuprofen oral suspension approved?**
The MHRA decided that the benefits of Ibuprofen oral suspension outweigh the identified risks and it was recommended that it be approved for use.
What measures are being taken to ensure the safe and effective use of Ibuprofen oral suspension?
A risk management plan (RMP) has been developed to ensure that Ibuprofen oral suspension is used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Ibuprofen oral suspension including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

Other information about Ibuprofen oral suspension
A Marketing Authorisation was granted in the UK on 13 October 2017.

The full PAR for Ibuprofen oral suspension follows this summary.

This summary was last updated in October 2017.
Table of Contents

I  Introduction  Page 6
II  Quality aspects  Page 7
III Non-clinical aspects  Page 8
IV  Clinical aspects  Page 8
V  User consultation  Page 9
VI  Overall conclusion, benefit/risk assessment and recommendation  Page 9

Table of content of the PAR update  Page 12
I Introduction

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Abbott Laboratories Limited a Marketing Authorisation for the medicinal product Ibuprofen 100 mg/5ml oral suspension (PL 00037/0677) on 13 October 2017. This product is a prescription only medicine (POM).

Ibuprofen 100 mg/5ml oral suspension is indicated for its analgesic and anti-inflammatory effects in the treatment of rheumatoid arthritis (including juvenile rheumatoid arthritis or Still's disease), ankylosing spondylitis, osteoarthritis and other non-rheumatoid (seronegative) arthropathies.

In the treatment of non-articular rheumatic conditions, Ibuprofen 100 mg/5ml oral suspension is indicated in peri-articular conditions such as frozen shoulder (capsulitis), bursitis, tendinitis, tenosynovitis and low back pain; Ibuprofen 100 mg/5ml oral suspension can also be used in soft-tissue injuries such as sprains and strains.

Ibuprofen 100 mg/5ml oral suspension is also indicated for its analgesic effect in the relief of mild to moderate pain such as dysmenorrhoea, dental and post-operative pain and for symptomatic relief of headache including migraine headache.

Ibuprofen 100 mg/5ml oral suspension is indicated in short-term use for the treatment of pyrexia in children over one year of age.

This application was made under Article 10c of Directive 2001/83/EC, as amended. The applicant has cross-referred to Brufen syrup authorised to Abbott Laboratories Limited (PL 00037/0339) on 15 February 2002. This licence underwent changes of ownership procedure to Mylan UK Healthcare Limited (PL 43900/0011) on 26 March 2015 and then to the current Marketing Authorisation Holder, Mylan Products Limited (PL 46302/0011), on 09 September 2016.

No new data were submitted nor were they necessary to be submitted for this application, as the data are identical to those of the previously authorised cross-reference product.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product type at all sites responsible for the manufacture and assembly of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application, and these are satisfactory.

No new or unexpected safety concerns arose during the review of information provided by the Marketing Authorisation Holder and it was, therefore, judged that the benefits of taking Ibuprofen 100 mg/5ml oral suspension outweigh the risks and a Marketing Authorisation was granted.
II QUALITY ASPECTS
II.1 INTRODUCTION
This is an informed consent application for Ibuprofen 100 mg/5ml oral suspension (PL 00037/0677) submitted under Article 10c of Directive 2001/83/EC, as amended.

The applicant has cross-referred to Brufen syrup authorised to Abbott laboratories Limited (PL 00037/0339) on 15 February 2002. This licence underwent changes of ownership procedure to Mylan UK Healthcare Limited (PL 43900/0011) on 26 March 2015 and then to the current Marketing Authorisation Holder, Mylan Products Limited (PL 46302/0011), on 09 September 2016. The application is considered valid.

MARKETING AUTHORISATION APPLICATION FORM
Name(s)
The proposed name of the product is Ibuprofen 100 mg/5ml oral suspension. The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes
Each 5ml of Ibuprofen 100mg/5ml oral suspension contains 100mg ibuprofen. The route of administration is oral.

The product is packaged in an amber-coloured polyethylene terephthalate (PET) bottle with an aluminium cap fitted with a low-density polyethylene liner. The pack size is 500 ml.

The proposed shelf-life for the product is 36 months with storage conditions “Store below 25°C” and “protect from light”. Once the bottle is opened, the product should be used within 12 months.

The packaging, proposed shelf-life and storage conditions are consistent with the details registered for the cross-reference product.

Legal status
The product is available as a prescription only medicine (POM).

Marketing Authorisation Holder/Contact Persons/Company
Abbott Laboratories Limited, Abbott House, Vanwall Business Park, Vanwall Road Maidenhead, Berkshire, SL6 4XE, UK

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory Curriculum Vitae (CV) has been provided.

Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

**Manufacturing process**
The proposed manufacturing process is consistent with the details registered for the cross-reference product.

**Finished product/shelf-life specifications**
The proposed finished product specification is in line with the details registered for the cross-reference product.

**Bioequivalence**
No bioequivalence data are required to support this simple application as the proposed product is manufactured to the same formula and uses the same process as the reference product Brufen syrup (Mylan Products Limited; PL 46302/0011).

**EXPERT REPORT**
The applicant cross-refers to the data for Brufen syrup (Mylan Products Limited; PL 46302/0011), to which this application is claimed to be identical. This is acceptable. The applicant has included expert reports for the application. Signed declarations and copies of the experts’ CVs are enclosed for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

**II.4 Discussion on chemical, pharmaceutical and biological aspects**
The quality data for this application is consistent with those approved for Brufen syrup (Mylan products Limited; PL 46302/0011) and, as such, have been judged to be satisfactory. The grant of a Marketing Authorisation is recommended.

**III NON-CLINICAL ASPECTS**
As this is an abridged simple application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data has been supplied and none are required.

A suitable justification has been provided for not submitting an environmental risk assessment.

The grant of a Marketing Authorisation is recommended.

**IV CLINICAL ASPECTS**
As this is an abridged simple application submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

A summary of the pharmacovigilance system has been provided with this application.

**Risk Management Plan (RMP)**
The applicant has submitted an RMP, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to
Ibuprofen 100 mg/5ml oral suspension.

**A summary of safety concerns and routine risk minimisation as approved in the RMP, is listed below:**

<table>
<thead>
<tr>
<th>Safety Concern</th>
<th>Routine Risk Minimization Measures</th>
<th>Additional Risk Minimization Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal bleeding, ulceration and perforation</td>
<td>Routine pharmacovigilance. Risk addressed in proposed SmPC sections 4.3, 4.4, 4.5, 4.8, and 4.9.</td>
<td>Not planned</td>
</tr>
<tr>
<td>Cardiovascular Risk</td>
<td>Routine pharmacovigilance. Risk addressed in proposed SmPC sections 4.3, 4.4, 4.8, and 4.9.</td>
<td>Not planned</td>
</tr>
<tr>
<td>Severe skin reactions</td>
<td>Routine pharmacovigilance. Risk addressed in proposed SmPC sections 4.4 and 4.8.</td>
<td>Not planned</td>
</tr>
<tr>
<td>Renal disorders</td>
<td>Routine pharmacovigilance. Risk addressed in proposed SmPC sections 4.3, 4.4 and 4.8.</td>
<td>Not planned</td>
</tr>
<tr>
<td>Interaction with low-dose aspirin</td>
<td>Routine pharmacovigilance. Risk addressed in proposed SmPC sections 4.4 and 4.5.</td>
<td>Not planned</td>
</tr>
<tr>
<td>Patent Ductus Arteriosus</td>
<td>Regular awareness</td>
<td>Not planned</td>
</tr>
</tbody>
</table>

Routine risk minimisation is provided through the Summary of Product Characteristics and the Patient Information Leaflet (PIL) and this is sufficient.

The grant of a Marketing Authorisation is recommended.

V **USER CONSULTATION**

A user consultation with target patient groups on the PIL has been performed on the basis of a bridging report making reference to the leaflet for Brufen Syrup (Mylan Products Ltd; PL 46302/0011). The bridging report submitted by the applicant is acceptable.

VI **OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION**

The quality of the product is acceptable, and no new non-clinical or clinical concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with ibuprofen is considered to have demonstrated the therapeutic value of the compound. The benefit/risk assessment is, therefore, considered to be positive.
Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for Ibuprofen 100 mg/5ml oral suspension is presented below:
Ibuprofen 100 mg/5ml oral suspension

Each 5 ml contains 100 mg Ibuprofen. Also contains propyl hydroxybenzoate (E216), methyl hydroxybenzoate (E218), sorbitol (E420), turmeric yellow (E100) and sucrose. For oral use as directed by a doctor.

Read the package leaflet before use.

Keep out of the reach and sight of children.

Shake well before use.

Once opened, use within 12 months.

Store below 25°C and protect from light.

Abbott Laboratories Limited
Abbott House, Verwell Business Park,
Verwell Road, Maidenhead, Berkshire,
SL6 4XE, UK

PL 00037/0677

IBUPROFEN
100mg/5ml
oral suspension
Ibuprofen 100 mg/ 5 ml

500 ml
Table of content of the PAR update

Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitment)

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>