Public Assessment Report

UKPAR

Ibuprofen 200 mg, 400 mg and 600 mg Film-coated Tablets

(Ibuprofen)

UK Licence No: PL 21880/0175-7 & 0189

Medreich plc
LAY SUMMARY
Ibuprofen 200 mg, 400 mg and 600 mg Film-coated Tablets
(Ibuprofen)

This is a summary of the Public Assessment Report (PAR) for Ibuprofen 200 mg, 400 mg and 600 mg Film-coated Tablets (PL 21880/0175-7 & 0189). Ibuprofen 200 mg, 400 mg and 600 mg Film-coated Tablets will be referred to as Ibuprofen tablets throughout this lay summary, for ease of reading.

This summary explains how Ibuprofen tablets were assessed and their authorisation recommended, as well as the conditions of use. It is not intended to provide practical advice on how to use Ibuprofen tablets.

For practical information about using Ibuprofen tablets, patients should read the Patient Information Leaflets (PILs) or contact their doctor or pharmacist.

What are Ibuprofen tablets and what are they used for?
Ibuprofen tablets are ‘generic medicines’. This means that these products are similar to ‘reference medicines’, already authorised in the European Union (EU) called Brufen 200 mg, 400 mg and 600 mg tablets (PL 00037/0333-0335; Abbott Laboratories Limited).

Ibuprofen 200mg Film-coated Tablets (available from pharmacy) are used for the relief of mild to moderate pain including rheumatic and muscular pain, backache, headache, dental pain, migraine, neuralgia, period pain, fever and cold and flu symptoms.

Ibuprofen 200mg Film-coated Tablets (available on general sale list) are used for the relief of mild to moderate pain including rheumatic and muscular pain, pain of some arthritic conditions backache, headache, dental pain, migraine, neuralgia, period pain, feverishness and the symptoms of cold and flu.

Ibuprofen 400 mg Tablets are used for the relief of mild to moderate pain including rheumatic and muscular pain, pain of some arthritic conditions, backache, neuralgia, migraine, headache, dental pain, period pains, feverishness and the symptoms of cold and flu.

Ibuprofen 600 mg Tablets 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. They can also be used to treat other painful conditions such as toothache, pain after operations, period pain and headache, including migraine.

How do Ibuprofen tablets work?
Ibuprofen (the active ingredient in this medicine) belongs to a group of medicines known as non-steroidal anti-inflammatory drugs (NSAIDs) which relieve pain, reduce swelling and lower temperature when the patient has a fever.

How are Ibuprofen tablets used?
Ibuprofen tablets are taken orally with or after food, with a glass of water. The whole tablet should be swallowed and not chewed, broken, crushed or sucked to help prevent discomfort in the mouth or irritation in the throat.

This product is intended for short term use only. Patients should take the lowest dose for the shortest time necessary to relieve the symptoms. This medicine should not be taken for longer than 10 days unless advised by a doctor.
The recommended dosage of Ibuprofen 200 mg Film-coated Tablets in adults, the elderly and children over 12 years is 1 to 2 tablets up to 3 times a day. The shortest time between doses must be at least 4 hours and no more than 6 tablets should be taken in any 24 hour period.

The recommended dosage of Ibuprofen 400 mg Film-coated Tablets in adults, the elderly and children over 12 years is 1 tablet up to three times a day as required. The shortest time between doses must be at least 4 hours and no more than 3 tablets should be taken in any 24 hour period.

Ibuprofen 400 is not recommended in children under 12 years old except on the advice of a doctor.

The usual dosage of Ibuprofen 600 mg Film-coated Tablets in adults is 600 to 1800 mg spread throughout the day. A doctor may choose to increase this depending on what patients are being treated for, but no more than 2400 mg should be taken in a day.

The usual daily dosage is 20 mg per kg of bodyweight, given in divided doses. Ibuprofen 600 mg Tablets should NOT be taken by children weighing less than 7 kg.

In cases of severe juvenile arthritis a doctor may increase the dosage up to 40 mg/kg in divided doses.

These medicinal products can be either obtained with a prescription (600 mg tablets) or are available on General Sale List (GSL) (200 mg tablets) and from pharmacy (200 mg and 400 mg tablets).

Please read Section 3 of the PILs for detailed information on dosing recommendations, the route of administration and the duration of treatment.

**How has Ibuprofen tablets been studied?**
Because Ibuprofen tablets are generic medicines, studies in patients have been limited to tests to determine that they are bioequivalent to the reference medicines, Brufen 200 mg, 400 mg and 600 mg Tablets. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

**What are the benefits and risks of Ibuprofen tablets?**
Because Ibuprofen tablets are generic medicines, and are bioequivalent to the reference medicines, Brufen 200 mg, 400 mg and 600 mg tablets, their benefits and risks are taken as being the same as the reference medicines.

**Why are Ibuprofen tablets approved?**
It was concluded that, in accordance with EU requirements, Ibuprofen tablets have been shown to have comparable quality and to be bioequivalent to Brufen 200 mg, 400 mg and 600 mg tablets. Therefore, the view was that, as for Brufen 200 mg, 400 mg and 600 mg tablets, the benefits outweigh the identified risks.

**What measures are being taken to ensure the safe and effective use of Ibuprofen tablets?**
A risk management plan has been developed to ensure that Ibuprofen tablets are used as safely as possible. Based on this plan, safety information has been included in the Summaries of Product Characteristics (SmPCs) and the PILs for Ibuprofen tablets, 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 and healthcare professionals will be monitored and reviewed continuously as well.
Other information about Ibuprofen tablets
Marketing Authorisations were granted in the UK on 03 August 2016.

The full PAR for Ibuprofen tablets follows this summary.

For more information about treatment with Ibuprofen tablets, read the PILs or contact your doctor or pharmacist.

This summary was last updated in September 2016.
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I Introduction

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) granted Medreich plc Marketing Authorisations for the medicinal products Ibuprofen 200 mg, 400 mg and 600 mg Film-coated Tablets (PL 21880/0175-0177 & 0189). The products are either available on prescription only medicine (POM) or are available on General Sale List (GSL) or pharmacy (P). These medicinal products are indicated for:

Ibuprofen 200mg Film-coated Tablets (P) for the relief of mild to moderate pain including rheumatic and muscular pain, backache, headache, dental pain, migraine, neuralgia, period pain, fever and cold and flu symptoms.

Ibuprofen 200mg Film-coated Tablets (GSL) for the relief of mild to moderate pain including rheumatic and muscular pain, pain of some arthritic conditions backache, headache, dental pain, migraine, neuralgia, period pain, feverishness and the symptoms of cold and flu.

Ibuprofen 400mg Film-coated Tablets for the relief of mild to moderate pain including rheumatic and muscular pain, pain of some arthritic conditions, backache, neuralgia, migraine, headache, dental pain, period pains, feverishness and the symptoms of cold and flu.

Ibuprofen 600 mg Tablets are 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. They can also be used to treat other painful conditions such as toothache, pain after operations, period pain and headache, including migraine.

These applications were submitted under Article 10(1) of Directive 2001/83/EC, as amended, claiming to be generic medicinal products. The applicant has cross referred to Brufen 200 mg, 400 mg and 600 mg tablets, which were first authorised to Knoll Pharma Limited (PL 13530/0005-0007) on 01 April 1993. These licences underwent change of ownership procedures, firstly to Knoll Limited (PL 00169/0049-0051) on 21 July 1995, and then to the current Marketing Authorisation Holder (MAH), Abbot Laboratories Limited (PL 00037/0333-0335), on 15 February 2002.

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

No new non-clinical studies were conducted, which is acceptable given that the applications were based on being generic medicinal products of originator products that have been licensed for over 10 years.

With the exception of one bioequivalence study, no new clinical data were provided with these applications. A bioequivalence study was submitted to support these applications, comparing the applicant’s test product Ibuprofen 600 mg tablets with the reference product Brufen (Ibuprofen) 600 mg Tablets (Abbott Laboratories Ltd., UK) in healthy human adult subjects, under fasting conditions. The bioequivalence study was conducted in line with current Good Clinical Practice (GCP).

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 manufacturing and assembly of these products. Evidence of compliance with GMP has been provided for the named manufacturing and assembly sites.

A summary of the pharmacovigilance system and a detailed risk management plan have been provided with these applications 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 200 mg, 400 mg and 600 mg Film-coated Tablets outweigh the risks and Marketing Authorisations were granted.
II  Quality Aspects

II.1  Introduction

Ibuprofen 200 mg, 400 mg and 600 mg Film-coated Tablets are formulated as white to off-white, pillow-shaped, film-coated tablets with plain on both sides.

Each film-coated tablet contains 200 mg, 400 mg and 600 mg of ibuprofen, as active ingredient. The excipients are sodium lauryl sulphate, croscarmellose sodium, lactose monohydrate, microcrystalline cellulose, povidone, colloidal anhydrous silica, stearic acid making up the tablet core, and the tablet coat is composed of hypromellose, macrogol 6000, purified talc and titanium dioxide (E-171).

All excipients comply with their respective European Pharmacopoeia monographs. Satisfactory Certificates of Analysis have been provided for all excipients showing compliance with their proposed specifications.

The only excipient used that contains material of animal or human origin is lactose monohydrate. The applicant has provided a declaration that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption.

No genetically modified organisms (GMO) have been used in the preparation of these excipients.

The 200 mg tablets, available on GSL, are packaged in aluminium polyvinylchloride blisters containing 12 and 16 tablets.

The 200 mg tablets, supplied though a pharmacy, are packaged in aluminium polyvinylchloride blisters containing 24, 48, 84 and 96 tablets.

The 400 mg tablets are packaged either in aluminium-polyvinylchloride blisters containing 12, 24, 48, 84 and 96 tablets or in a high density polyethylene container with a pack size of 100 tablets.

The 600 mg tablets are packaged either in aluminium-polyvinylchloride blister containing 84 tablets or in a high density polyethylene container with a pack size of 500 tablets.

Not all pack sizes may be marketed.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components.

II.2  Drug Substance

INN: Ibuprofen

Chemical names: (2RS)-2-[4-(2-Methylpropyl)phenyl]propanoic acid.

Structural formula: 

Molecular formula: \( C_{13}H_{18}O_2 \)
Molecular mass: 206.3 g/mol

Appearance: White or almost white, crystalline powder or colourless crystals.

Solubility: Practically insoluble in water, freely soluble in acetone, in methanol and in dichloromethane. It dissolves in dilute solutions of alkali hydroxides and carbonates.
Ibuprofen is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance, ibuprofen, are covered by the European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificates of Suitability.

II.3. Medicinal Product
Pharmaceutical Development
The objective of the development programme was to formulate safe, efficacious tablets containing 200, 400 mg and 600 mg of ibuprofen per tablet, that are generic versions of the reference products Brufen (Ibuprofen) 200 mg, 400 mg and 600 mg Tablets (Abbott Laboratories Ltd., UK).

Comparative in-vitro dissolution and impurity profiles have been provided for the proposed and originator products.

The applicant has requested a waiver from performing bioequivalence studies on the 200 mg and 400 mg strength tablets on the basis that the tablets are proportionally formulated; they have a similar formulation to the reference product and the three strengths demonstrate similar dissolution profiles.

Manufacture of the products
Satisfactory batch formulae have been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated using the minimum commercial scale batch sizes and has shown satisfactory results. The applicant has committed to perform further process validation on full scale commercial-scale batches of each tablet strength post approval.

Finished Product Specifications
The finished product specifications proposed are acceptable. The test methods have been described that have been adequately validated. Batch data have been provided that comply with the release specification. Certificates of Analysis have been provided for all working standards used.

Stability of the Products
Finished product stability studies were performed in accordance with current guidelines on batches of finished product in the packaging proposed for marketing. The data from these studies support a shelf-life of 24 months with no special storage conditions. The content must be discarded 6 months after opening.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

II.4 Discussion on chemical, pharmaceutical and biological aspects
There are no objections to the approval of these applications from a pharmaceutical viewpoint.

III Non-Clinical Aspects
III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of ibuprofen are well-known, no new non-clinical studies are required and none have been provided. An overview based on the literature review is, thus, appropriate.

The applicant’s non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.
III.2 Pharmacology
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.3 Pharmacokinetics
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.4 Toxicology
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.5 Ecotoxicity/environmental risk assessment (ERA)
Since Ibuprofen 200 mg, 400 mg and 600 mg Film-coated Tablets are intended for generic substitution, their use will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects
No new non-clinical studies were conducted, which is acceptable given that the applications were based on being generic medicinal products of the originator products that have been licensed for over 10 years.

There are no objections to the approval of these applications from a non-clinical viewpoint.

IV Clinical Aspects
IV.1 Introduction
The clinical pharmacology of ibuprofen is well-known. With the exception of data from the bioequivalence study detailed below, no new pharmacodynamics or pharmacokinetic data are provided or are required for these applications.

No new efficacy or safety studies have been performed and none are required for this type of applications. A comprehensive review of the published literature has been provided by the applicant, citing the well-established clinical pharmacology, efficacy and safety of ibuprofen.

A bioequivalence study was conducted on Ibuprofen 600 mg Tablets, a waiver from additional bioequivalence studies was requested for Ibuprofen 200 mg and 400 mg Tablets.

Based on the data provided, Ibuprofen 200 mg, 400 mg and 600 mg Film-coated Tablets can be considered to be bioequivalent to Brufen 200 mg, 400 mg and 600 mg Tablets (Abbott Laboratories Ltd., UK).

IV.2 Pharmacokinetics
In support of these applications the Marketing Authorisation holder has submitted results from the following bioequivalence study:

A randomised, open-label, two treatment, two period, two sequence, single dose, crossover, bioequivalence study comparing the pharmacokinetics of the test product Ibuprofen 600 mg Film-coated Tablets with the reference product Brufen 600 mg Tablets (Abbott Laboratories Ltd., UK) in healthy adult subjects, under fasting conditions.

Subjects received the test or reference treatment after an overnight fast of at least 8 hours. Blood samples were collected at pre-dose and up to and including 16:00 hours post dose. A washout period of 7 days was kept between the two treatment periods.
Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, tmax median, range)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>$AUC_{0-t}$ µg/ml/h</th>
<th>$AUC_{0-\infty}$ µg/ml/h</th>
<th>$C_{max}$ µg/ml</th>
<th>$t_{max}$ h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td>171.64 ± 38.602</td>
<td>173.76 ± 39.106</td>
<td>46.96 ± 11.994</td>
<td>2.00 (0.50-4.00)</td>
</tr>
<tr>
<td>Reference</td>
<td>169.61 ± 32.821</td>
<td>171.67 ± 33.400</td>
<td>45.36 ± 8.144</td>
<td>2.00 (0.75-5.00)</td>
</tr>
</tbody>
</table>

*Ratio (90% CI)

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</thead>
<tbody>
<tr>
<td>$AUC_{0-t}$</td>
<td>100.05</td>
<td>(97.05 to 103.15)</td>
<td>100.05</td>
<td>(97.05 to 103.15)</td>
</tr>
<tr>
<td>$AUC_{0-\infty}$</td>
<td>100.12</td>
<td>(97.13 to 103.20)</td>
<td>100.12</td>
<td>(97.13 to 103.20)</td>
</tr>
<tr>
<td>$C_{max}$</td>
<td>101.01</td>
<td>(93.65 to 108.94)</td>
<td>101.01</td>
<td>(93.65 to 108.94)</td>
</tr>
</tbody>
</table>

*ln-transformed values

Conclusion
The 90% confidence intervals of the test/reference ratio for $AUC$ and $C_{max}$ values lie within the acceptable limits of 80.00% to 125.00%, in line with the ‘Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr**). Bioequivalence has been shown for the test formulation (Ibuprofen 600 mg Film-coated Tablets) and the reference formulation (Brufen 600 mg Tablets) under fasting conditions.

As the 200 mg and 400 mg strength test products meet the biowaiver criteria specified in the current bioequivalence guidance, the results and conclusions of the bioequivalence study with the 600 mg tablet strength can be extrapolated to the 200 mg and 400 mg strength tablets.

IV.3 Pharmacodynamics
No new pharmacodynamics data are required for these applications and none have been submitted.

IV.4 Clinical efficacy
No new clinical efficacy data are required for these applications and none have been submitted.

IV.5 Clinical safety
No new clinical safety data are required for these applications and none have been submitted.

IV.6 Risk Management Plan (RMP) and Pharmacovigilance system
The Marketing Authorisation holder 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 600 mg Film-coated Tablets.
A summary of safety concerns and planned risk minimisation activities, as approved in the RMP, is listed below:

<table>
<thead>
<tr>
<th>Safety Concern</th>
<th>Routine Risk Minimisation Measures</th>
<th>Additional Risk Minimisation Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal perforation, ulceration and bleeding (PUB)</td>
<td>The risks of gastrointestinal perforation, ulceration and bleeding (PUB) associated with use of drug product are described in the SPC Sections 4.2, 4.3, 4.4, 4.5 and 4.8 and PIL Sections 2, 3, 4, and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Premature closure of the foetal ductus arteriosus (use during third trimester of pregnancy)</td>
<td>The risk of premature closure of the foetal ductus arteriosus associated with use of the drug product during third trimester of pregnancy is described in the SPC Sections 4.3, 4.6 and PIL Section 2, and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
</tr>
<tr>
<td>Hypersensitivity reactions in patients with previous hypersensitivity reactions to NSAIDs or aspirin</td>
<td>The risk of hypersensitivity reactions associated with use of the drug product in patients with previous hypersensitivity reactions to NSAIDs or aspirin are described in the SPC Sections 4.3, 4.4, 4.8, and PIL Sections 2, 4, and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Bronchospasm in patients with asthma or allergic disease</td>
<td>The risk of bronchospasm associated with use of the drug product in patients with asthma</td>
<td>None</td>
</tr>
<tr>
<td>Safety Concern</td>
<td>Routine Risk Minimisation Measures</td>
<td>Additional Risk Minimisation Measures</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------</td>
</tr>
<tr>
<td>Arterial thrombotic events (MI and stroke) – (at doses ≥ 2400 mg/day)</td>
<td>The risks of arterial thrombotic events (MI and stroke) associated with use of the drug product at doses ≥ 2400 mg/day is described in the SPC Sections 4.3, 4.4, 4.8, and PIL Sections 2, 4, and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Cardio-renal effects</td>
<td>The risks of cardio-renal effects associated with use of the drug product are described in the SPC Section 4.4 and PIL Section 2 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Coagulation disorders</td>
<td>The risk of coagulation disorders associated with use of the drug product is described in the SPC Sections 4.3, 4.4, 4.5, 4.8, and PIL Sections 2 and 4, and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
</tr>
<tr>
<td>Serious skin reactions including Stevens Johnson syndrome and toxic epidermal necrolysis</td>
<td>The risks of serious skin reactions including Stevens Johnson syndrome and toxic epidermal necrolysis associated with use of the drug product are described in the SPC Sections 4.4, 4.8, and PIL Section 4, and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Renal disorders</td>
<td>The risks of renal disorders associated with use of the drug product are described in the SPC Sections 4.3, 4.4, 4.8, and PIL.</td>
<td>None</td>
</tr>
</tbody>
</table>
### Safety Concern

<table>
<thead>
<tr>
<th>Safety Concern</th>
<th>Routine Risk Minimisation Measures</th>
<th>Additional Risk Minimisation Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen 200 mg, 400 mg and 600 mg Film-coated Tablets</td>
<td>Sections 2, 4, and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td></td>
</tr>
<tr>
<td>Hepatic disorders</td>
<td>The risks of hepatic disorders associated with use of the drug product is described in the SPC Sections 4.3, 4.4, 4.8, and PIL Sections 2, 4 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
</tbody>
</table>

#### Important Potential Risks

- **Foetal cardiac malformation, gastroschisis and miscarriage (use during early pregnancy)**
  - The risks of foetal cardiac malformation, gastroschisis and miscarriage associated with use of the drug product in early pregnancy are described in the SPC Section 4.6, and PIL Section 2 and appropriate advice is provided to the prescriber to minimise these risks
  - None

#### Missing Information

- **Use during breast feeding**
  - The SPC Section 4.6 and PIL Section 2, clearly states that, in the limited studies so far available, NSAIDs can appear in the breast milk in very low concentrations. NSAIDs should, if possible, be avoided when breastfeeding.
  - None

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### IV.7 Discussion on the clinical aspects

The grant of Marketing Authorisations is recommended for these applications.

### V User consultation

The package leaflet has been evaluated via a user consultation study, in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC, as amended. The language used for the purpose of user testing the PIL was English.

The results show that the package leaflet meets the criteria for readability, as set out in the *Guideline on the readability of the label and package leaflet of medicinal products for human use.*
VI Overall conclusion, benefit/risk assessment and recommendation
The quality of the products is acceptable, and no new non-clinical or clinical concerns have been identified. The data provided by the applicant showed that the test products are comparable to the reference products. Extensive clinical experience with ibuprofen is considered to have demonstrated the therapeutic value of the compounds. 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 200 mg, 400 mg and 600 mg Film-coated Tablets is presented below:
Ibuprofen 200mg Film-coated tablets

Read the package leaflet before use

INGREDIENTS
Each film coated tablet contains 200 mg Ibuprofen. Also contains Lactose monohydrate.

DOSAGE
For oral use. Swallow whole. Do not chew or crush.

WARNING

KEEP OUT OF THE SIGHT AND REACH OF CHILDREN

SPECIAL WARNINGS
Do not take if you
• have (or have had two or more episodes of) a stomach ulcer, perforation or bleeding
• are allergic to ibuprofen (or anything else in this medicine), aspirin or other related painkillers
• are taking other NSAID painkillers, or aspirin with a daily dose above 75mg
• are in the last 3 months of pregnancy
Talk to a pharmacist or your doctor before taking if you
• have asthma, diabetes, high cholesterol, high blood pressure, had a stroke, liver, heart, kidney or bowel problems
• are a smoker
• are pregnant
If symptoms do not get better or get worse or if you get new symptoms, talk to your doctor.
Ibuprofen 400mg Film-coated tablets

Read the package leaflet before use

INGREDIENTS
Each film coated tablet contains 400 mg ibuprofen. Also contains Lactose monohydrate.

DOSAGE
For oral use. Swallow whole. Do not chew or crush.

WARNING
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN
SPECIAL WARNINGS
Do not take if you
• have (or have had two or more episodes of) a stomach ulcer, perforation
• are allergic to ibuprofen (or anything else in this medicine), aspirin or other related painkillers
• are taking other NSAID painkillers or aspirin with a daily dose above 75mg
• are in the last 3 months of pregnancy

Talk to a pharmacist or your doctor before taking if you
• have asthma, diabetes, high cholesterol, high blood pressure, had a stroke, liver, heart, kidney or bowel problems
• are a smoker
• are pregnant
If symptoms do not get better or get worse or if you get new symptoms, talk to your doctor.
Ibuprofen 400mg Film-coated tablets

Read the package leaflet before use

INGREDIENTS
Each film coated tablet contains 400 mg ibuprofen. Also contains Lactose monohydrate.

DOSAGE
For oral use. Swallow whole. Do not chew or crush.

WARNING
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN
SPECIAL WARNINGS
Do not take if you have (or have had two or more episodes of) a stomach ulcer, perforation or bleeding.
- are allergic to ibuprofen (or anything else in this medicine), aspirin or other related painkillers
- are taking other NSAID painkillers or aspirin with a daily dose above 75 mg
- are in the last 3 months of pregnancy

Talk to a pharmacist or your doctor before taking if you have asthma, diabetes, high cholesterol, high blood pressure, had a stroke, liver, heart, kidney or bowel problems or are a smoker. If you are pregnant or get new symptoms, talk to your doctor.

MEDREICH PLC
Warwick House, Plane Tree Crescent, Feltham TW13 9JF, UK

48 Capsules-shaped tablets

Ibuprofen 400mg Film-coated tablets

48 Capsules-shaped tablets
**Ibuprofen 400mg Film-coated tablets**

**Read the package leaflet before use**

**INGREDIENTS**
Each film-coated tablet contains 400 mg Ibuprofen, also contains Lactose monohydrate.

**DOSAGE**
For oral use, Swallow whole. Do not chew or crush.

**WARNING**
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN

**SPECIAL WARNINGS**
Do not take if you have (or have had two or more episodes of)
1. a stomach ulcer, perforation or bleeding; • are allergic to ibuprofen (or anything else in this medicine), aspirin or other related painkillers • are taking other NSAID painkillers or aspirin with a daily dose above 75mg • are in the last 3 months of pregnancy

Talk to a pharmacist or your doctor before taking if you have asthma, diabetes, high cholesterol, high blood pressure, had a stroke, liver, heart, kidney or bowel problems • are a smoker • are pregnant
If symptoms do not get better or get worse or if you get new symptoms, talk to your doctor.

**Space for Barcode**

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**Medreich PLC**

Wandsworth House, Plane Tree Crescent, Fulham, SW6 7SH, UK

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**PL 21880/0175 & 0189**
Ibuprofen 400mg Film-coated tablets

Read the package leaflet before use

INGREDIENTS
Each film coated tablet contains 400mg Ibuprofen. Also contains Lactose monohydrate.

DOSAGE
For oral use. Swallow whole. Do not chew or crush.

WARNING
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN

SPECIAL WARNINGS
Do not take if you have (or have had two or more episodes of) a stomach ulcer, perforation, or bleeding.
• are allergic to ibuprofen (or anything else in this medicine), aspirin or other related painkillers
• are taking other NSAID painkillers or aspirin with a daily dose above 70mg
• are in the last 3 months of pregnancy
• have asthma, diabetes, high cholesterol, high blood pressure, had a stroke, liver, heart, kidney or bowel problems
• are a smoker
• are pregnant

Talk to a pharmacist or your doctor before taking if you
• have asthma, diabetes, high cholesterol, high blood pressure, had a stroke, liver, heart, kidney or bowel problems
• are a smoker
• are pregnant if symptoms do not get better or get worse or if you get new symptoms, talk to your doctor.

Ibuprofen 400mg Film-coated tablets

96 Capsules-shaped tablets

MEDREICH
INGREDIENTS
Each film coated tablet contains 600 mg Ibuprofen. Also contains Lactose monohydrate.

DOSAGE
For oral use. Swallow whole. Do not chew or crush.

WARNING
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN

Ibuprofen 600mg Film-coated tablets

Read the package leaflet before use.

MARA Holder
MEDREICH PLC
Wren's House, Pines Tree Crescent, Fulham, TW13 7EF, UK

Space for Barcode

24 Capsules-shaped tablets 200 mg

Ibuprofen 200mg Film-coated tablets

PL 21880/0177 & 0189

PL 21880/0175-0177

25
Ibuprofen 200mg Film-coated tablets

INGREDIENTS
Each film coated tablet contains 200 mg Ibuprofen. Also contains Lactose monohydrate.

DOSAGE
For oral use. Swallow whole. Do not chew or crush.

WARNING
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN
SPECIAL WARNINGS
Do not take if you
• have (or have had two or more episodes of) a stomach ulcer, perforation

or bleeding.
• are allergic to ibuprofen (or anything else in this medicine), aspirin or other related painkillers
• are taking other NSAID painkillers or aspirin with a daily dose above 75mg
• are in the last 3 months of pregnancy
Talk to a pharmacist or your doctor before taking if you
• have asthma, diabetes, high cholesterol, high blood pressure, had a stroke, liver, heart, kidney or bowel problems
• are a smoker
• are pregnant
If symptoms do not get better or get worse or if you get new symptoms, talk to your doctor.
PAR Ibuprofen 200 mg, 400 mg and 600 mg Film-coated Tablets

PL 21880/0175-0177 & 0189
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Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitment

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