Public Assessment Report

Decentralised Procedure

Ibuprofen 100 mg, chewable capsules, soft

Procedure No: UK/H/5319/001/DC

UK Licence No: PL 14338/0006

Banner Pharmacaps Europe B.V
LAY SUMMARY

Ibuprofen 100 mg, chewable capsules, soft
(ibuprofen; chewable capsules, soft; 10 mg)

This is a summary of the Public Assessment Report (PAR) for Ibuprofen 100 mg, chewable capsules, soft (PL 14338/0006; UK/H/5319/001/DC). It explains how Ibuprofen 100 mg, chewable capsules, soft were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use Ibuprofen 100 mg, chewable capsules, soft.

For practical information about using Ibuprofen 100 mg, chewable capsules, soft, patients or their carers should read the package leaflet or contact their doctor or pharmacist.

Ibuprofen 100 mg, chewable capsules, soft may be referred to as Ibuprofen 100 mg in this report.

What is Ibuprofen 100 mg and what is it used for?
Ibuprofen 100 mg is a medicine that contains the active substance ibuprofen. Ibuprofen 100 mg is used in patients 7 years and older for the symptomatic treatment of mild to moderate pain such as headache, period pain, dental pain and fever and pain associated with the common cold.

Ibuprofen 100 mg is a 'hybrid' medicine. This means that Ibuprofen 100 mg is similar to reference medicines already authorised in the European Union (EU) called Nurofen 200 mg Tablets (PL 00063/0385; Reckitt Benckiser Healthcare (UK) Limited) and Nurofen for children 100mg/5ml oral suspension (PL 00063/0665; Reckitt Benckiser Healthcare (UK) Limited).

How is Ibuprofen 100 mg used?
Ibuprofen 100 mg is taken by mouth. The capsules should be chewed and then swallowed. The capsules can be taken with or without liquid. This medicine is for short term use only.

The minimum effective dose should be used for the shortest time necessary to relieve symptoms.

Ibuprofen 100mg should not be given to children under 7 years of age.
The recommended dose is:

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger than 7 years</td>
<td>Do not give to children under 7 years of age</td>
</tr>
<tr>
<td>7 years – 9 years</td>
<td>Two capsules 3 times in 24 hours*</td>
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<tr>
<td>10 years – 12 years</td>
<td>Three capsules 3 times in 24 hours*</td>
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<tr>
<td>Over 12 years</td>
<td>Two to four capsules up to 3 times a day. Do not take more than 12 capsules in 24 hours.</td>
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*Doses should be given approximately every 6 to 8 hours, (or with a minimum of 6 hours between each dose if required).

A doctor should be consulted if symptoms persist or worsen for more than 10 days in those aged over 12 years. For children aged 7 years to 12 years, a doctor should be contacted if symptoms persist or worsen after 3 days.

For further information on how Ibuprofen 100mg is used, please see the Patient Information Leaflet and Summary of Product Characteristics available on the MHRA website.

Ibuprofen 100 mg can be obtained without a prescription.
How does Ibuprofen 100 mg work?
Ibuprofen 100 mg contains the active substance ibuprofen, which is a non-steroidal anti-inflammatory (NSAID) painkiller.

How has Ibuprofen 100 mg been studied?
As Ibuprofen 100 mg is a hybrid medicine, studies in patients have been limited to tests to determine that it is therapeutically equivalent to the reference medicines, Nurofen 200 mg Tablets (PL 00063/0385; Reckitt Benckiser Healthcare (UK) Limited) and Nurofen for children 100mg/5ml oral suspension (PL 00063/0665; Reckitt Benckiser Healthcare (UK) Limited). Two medicines are therapeutically equivalent when they produce the same measure of therapeutic effect in the body.

In addition, the company (Banner Pharmacaps Europe B.V) provided data from the published literature on ibuprofen.

What are the benefits and risks of Ibuprofen 100 mg?
Because Ibuprofen 100 mg is a hybrid medicine and is therapeutically equivalent to the reference medicines, its benefits and risks are taken as being the same as those of the reference medicines.

Why is Ibuprofen 100 mg approved?
It was concluded that, in accordance with EU requirements, Ibuprofen 100 mg has been shown to have comparable quality and to be therapeutically equivalent to Nurofen 200 mg Tablets (PL 00063/0385; Reckitt Benckiser Healthcare (UK) Limited) and Nurofen for children 100mg/5ml oral suspension (PL 00063/0665; Reckitt Benckiser Healthcare (UK) Limited) when administered at the same dose. Therefore, the view was that, as for Nurofen 200 mg Tablets (PL 00063/0385; Reckitt Benckiser Healthcare (UK) Limited) and Nurofen for children 100mg/5ml oral suspension (PL 00063/0665; Reckitt Benckiser Healthcare (UK) Limited), the benefits outweigh the identified risks.

What measures are being taken to ensure the safe and effective use of Ibuprofen 100 mg?
A Risk Management Plan has been developed to ensure that Ibuprofen 100 mg 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 100 mg, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Ibuprofen 100 mg.
A Marketing Authorisation was granted in the UK on 14 November 2013.

The full PAR for Ibuprofen 100 mg follows this summary.

For more information about treatment with Ibuprofen 100 mg read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in January 2014.
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Module 1
Information about the initial procedure

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Ibuprofen 100 mg, chewable capsules, soft</th>
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<tbody>
<tr>
<td>Type of Application</td>
<td>Hybrid, Article 10(3)</td>
</tr>
<tr>
<td>Active Substance(s)</td>
<td>Ibuprofen</td>
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<tr>
<td>Form</td>
<td>Chewable capsule, soft</td>
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<tr>
<td>Strength</td>
<td>100 mg</td>
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<td>MA Holder</td>
<td>Banner Pharmacaps Europe B.V.</td>
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<td>5048 AS Tilburg</td>
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<td>The Netherlands</td>
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<td>Reference Member State (RMS)</td>
<td>UK</td>
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<td>Concerned Member States (CMS)</td>
<td>The Netherlands</td>
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<td>Procedure Number</td>
<td>UK/H/5319/001/DC</td>
</tr>
<tr>
<td>Timetable</td>
<td>Day 210 – 03 October 2013</td>
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</table>
Module 2
Summary of Product Characteristics

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
Module 3
Patient Information Leaflet

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
Module 4
Labelling

Ibuprofen 100mg chewable capsules, soft

Each capsule contains 100 mg ibuprofen. Contains glucose, sucrose. See leaflet for further information.

Barrier Pharmacaps Europe B.V.
De Postbusmaat 7, 5246 AE Tilburg
The Netherlands
PL 14335/006

Ibuprofen 100mg chewable capsules, soft

Ibuprofen

16 chewable capsules, soft

Ibuprofen 100mg chewable capsules, soft

KEEP OUT OF SIGHT AND REACH OF CHILDREN.

If symptoms persist or worse than 2 days or if new symptoms appear:

- Consult your doctor.
- Keep products out of reach of children.

If you are allergic to ibuprofen or any of the other ingredients:

- You may have a different reaction.
- Consult your doctor.

If you use ibuprofen for more than 5 days:

- Consult your doctor.
- Keep products out of reach of children.

If you have kidney or liver problems:

- Consult your doctor.
- Keep products out of reach of children.

If you are on other medicine:

- Consult your doctor.
- Keep products out of reach of children.

If you have more episodes:

- Consult your doctor.
- Keep products out of reach of children.

If you are on other medicine:

- Consult your doctor.
- Keep products out of reach of children.

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Module 5
Scientific discussion during the initial procedure

I  INTRODUCTION
Based on the review of the data on quality, safety and efficacy, the UK and the Netherlands considered that the application for Ibuprofen 100 mg, chewable capsules, soft (PL 14338/0006; UK/H/5319/001/DC could be approved. This is a pharmacy (P) medicine, available only from pharmacies, indicated for the symptomatic treatment of mild to moderate pain such as headache, period pain, dental pain and fever and pain associated with the common cold.

The application was submitted using the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS), and the Netherlands as Concerned Member State (CMS). The application was submitted under Article 10(3) of Directive 2001/83/EC, as amended, as a hybrid application.

The application refers to the reference products Nurofen 200 mg Tablets (PL 00063/0385; Reckitt Benckiser Healthcare (UK) Limited) and Nurofen for children 100mg/5ml oral suspension (PL 00063/0665; Reckitt Benckiser Healthcare (UK) Limited), which were first approved in the UK to Crookes Healthcare Limited on 15 July 2003 and 11 March 1998, respectively.

Nurofen 200 mg Tablets (PL 00327/0146; Crookes Healthcare Limited, UK) was a line extension application to the existing Nurofen 200mg Tablets (PL 00327/0004), which was granted in the UK based on a full application on 06 May 1983. Nurofen 200 mg Tablets (PL 00327/0146; Crookes Healthcare Limited, UK) underwent a change of ownership procedure to Reckitt Benckiser Healthcare (UK) Limited (PL 00063/0385) on 29 January 2011. Nurofen for children 100mg/5ml oral suspension (PL 00327/0085) underwent a change of ownership procedure to Reckitt Benckiser Healthcare (UK) Limited (PL 00063/0665) on 07 July 2011.

The active ingredient, ibuprofen, is an analgesic, antipyretic and anti-inflammatory medication. It belongs to the class of agents commonly known as non-steroidal anti-inflammatory drugs (NSAIDs). There is evidence that the basic mechanism of pharmacological action of ibuprofen (like other NSAIDs) is the inhibition of prostaglandin biosynthesis. Prostaglandins are naturally occurring fatty acid derivatives that are widely distributed in the tissues. They are believed to be the common factor in the production of pain, fever, and inflammation.

A single-dose bioequivalence study was submitted to support this application, comparing the applicant’s test product Ibuprofen 100mg chewable soft gelatin capsule (200mg; 2 x 100mg chewable soft gelatin capsules) versus the reference products Nurofen 100mg/5ml oral suspension (200 mg; 1 x 10ml) and Nurofen 200mg tablet (200 mg; 1 x 200mg capsule) under fasting conditions.

With the exception of the bioequivalence study, no new non-clinical or clinical efficacy studies were performed for this application, which is acceptable given that this is a hybrid application based on an originator product that has been in clinical use for over 10 years.

The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place at all sites responsible for the manufacture, assembly and batch release of this product. For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.
For manufacturing sites outside the Community, the RMS has accepted copies of current GMP Certificates issued by the inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those non-Community sites.

The RMS and CMS considered that the application could be approved at the end of procedure (Day 210) on 03 October 2013. After a subsequent national phase, a licence was granted in the UK on 14 November 2013.

II. ABOUT THE PRODUCT

| Name of the product in the Reference Member State | Ibuprofen 100 mg, chewable capsules, soft |
| Name(s) of the active substance(s) (INN) | Ibuprofen |
| Pharmacotherapeutic classification (ATC code) | Propionic acid derivative NSAID (ATC code: M01A E01) |
| Pharmaceutical form and strength | Chewable capsule, soft; 100 mg |
| Reference number(s) for the Decentralised Procedure | UK/H/5319/001/DC |
| Reference Member State (RMS) | United Kingdom |
| Concerned Member States (CMS) | The Netherlands |
| Marketing Authorisation Number | PL 14338/0006 |
| Name and address of the authorisation holder | Banner Pharmacaps Europe B.V. De Posthoornstraat 7 5048 AS Tilburg The Netherlands |

III. SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 QUALITY ASPECTS

ACTIVE SUBSTANCE

INN: Ibuprofen
Chemical name(s): (2RS)-2-[4-(2-Methylpropyl)phenyl]propanoic acid; 2-(4-isobutylphenyl)propionic acid

Structure:

\[
\begin{array}{c}
\text{CH}_3 \\
\text{H}_5 \text{C} \\
\text{CH}_3 \\
\text{O}
\end{array}
\]

Molecular formula: \( \text{C}_{13}\text{H}_{18}\text{O}_2 \)
\( M_r = 206.3 \text{g/mol} \)
Appearance: White crystalline powder or colourless crystals.
Solubility: Practically insoluble in water and freely soluble in acetone, methanol and methylene chloride. 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 a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.
MEDICINAL PRODUCT

Other Ingredients
Other ingredients consist of the pharmaceutical excipients gelatin, purified water, liquid glucose, sucrose, fumaric acid (E297), sucralose, citric acid (E330), Acesulfame K (E950), disodium edetate, glycerin, Natural Orange Flavour and Opacode White NS-78-18011. Appropriate justification for the inclusion of each excipient has been provided.

Natural Orange Flavour contains (R)-p-mentha-1,8-diene (d-limonene), ethyl acetate and Alpha-pinene. Opacode White NS-78-18011 contains purified water, titanium dioxide (E171), propylene glycol, isopropyl alcohol and HPMC 2910/hypromellose 3cP (E464).

All excipients comply with their respective European Pharmacopoeia monographs with the exception of fumaric acid (E297), Natural Orange Flavour (and its constituents) and Opacode White NS-78-18011 (and its constituents). Fumaric acid (E297) is compliant with its United States-National Formulary monograph. Lecithin is compliant with its National Formulary monograph. Natural Orange Flavour, Opacode White NS-78-18011 and their respective constituents are controlled to suitable in-house specifications. Natural Orange Flavour is also compliant with current EU Directives concerning the use of flavouring agents in food. Certificates of Analysis have been provided for all excipients, showing compliance with the proposed specification.

With the exception of gelatin, none of the excipients contain materials of animal or human origin. The suppliers of gelatin have provided Certificates of Suitability from the European Directorate for the Quality of Medicines and Healthcare (EDQM) to show that it is manufactured in line with current European guidelines concerning the minimising of risk of transmission of Bovine Spongiform Encephalopathy/Transmissible Spongiform Encephalopathies (BSE/TSE).

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

Pharmaceutical Development
The objective of the development programme was to formulate a safe, efficacious, stable chewable soft gelatin capsule comparable in performance to the marketed reference products Nurofen 100mg/5 ml oral suspension and Nurofen 200 mg Tablet.

Suitable pharmaceutical development data have been provided for this application.

Comparative in-vitro dissolution profiles have been provided for this product and the reference products.

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 with pilot-scale batches that have shown satisfactory results. The Marketing Authorisation Holder has committed to performing process validation studies on future full-scale production batches.

Control of Finished Product
The finished product specification is acceptable. Test methods have been described that have been validated adequately. Batch data have been provided, which comply with the release specification. Certificates of Analysis have been provided for all working standards used.

Container-Closure System
The capsules are packaged in polyvinylchloride/polyethylene/polyvinylidene chloride/aluminium (PVC/PE/PVDC/aluminium) blisters packed with the Patient Information Leaflet in cartons, in pack sizes of 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, or 32 soft chewable capsules.
Not all pack sizes may be marketed.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with current European regulations concerning materials in contact with foodstuff.

**Stability of the Product**
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 15 months, with the storage conditions ‘Do not store above 30°C.’

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

**Bioequivalence/Bioavailability**
Satisfactory Certificates of Analysis have been provided for the test and reference batches used in the bioequivalence study. The bioequivalence study is discussed in Section III.3, Clinical Aspects.

**Summary of Product Characteristics (SmPC), Product Information Leaflet (PIL) and Labels**
The SmPC, PIL and labels are satisfactory from a pharmaceutical perspective. Final text versions of the labelling and PIL have been provided. The Marketing Authorisation Holder has committed to submitting mock-ups to the relevant competent authorities for approval before marketing any pack size.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups (‘user testing’), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet 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 the leaflet contains.

**Marketing Authorisation Application (MAA) Form**
The MAA form is satisfactory from a pharmaceutical perspective.

**Expert Report (Quality Overall Summary)**
The quality overall summary has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

**Conclusion**
The grant of a Marketing Authorisation is recommended.

**III.2 NON-CLINICAL ASPECTS**
As the pharmacodynamic, pharmacokinetic and toxicological properties of ibuprofen are well-known, no new non-clinical data have been submitted and none are required.

The non-clinical overview has been written by an appropriately qualified person and is a suitable summary of the non-clinical aspects of the dossier.

The Marketing Authorisation Holder (MAH) has provided adequate justification for non-submission of an Environmental Risk Assessment. As the product is intended for substitution with a product that is already marketed, no increase in environmental burden is anticipated. Thus, the justification for non-submission of an Environmental Risk Assessment is accepted.

The grant of a Marketing Authorisation is recommended.
III.3 CLINICAL ASPECTS

Clinical Pharmacology

The clinical pharmacology of ibuprofen is well-known. With the exception of data from the bioequivalence study detailed below, no new pharmacodynamic or pharmacokinetic data are provided or required for this application.

In support of the application, the Marketing Authorisation Holder submitted the following bioequivalence study:

A randomised, open-label, single dose, 3-way crossover study comparing the applicant’s Ibuprofen 100 mg chewable soft gelatin capsule with the reference products Nurofen 100 mg/5 ml oral suspension (manufactured by Crookes Healthcare Limited, UK) and Nurofen 200 mg Tablet (manufactured by Crookes Healthcare Limited, UK) in healthy male subjects under fasting conditions.

The subjects were administered a single 200 mg dose of either the test (administered as 2 x 100 mg chewable soft gelatin capsules) or one of the reference products (1 x 10 ml of a 100 mg/5 ml oral suspension, or 1 x 200 mg tablet), after an overnight fast of at least 10 hours. Blood sampling was performed pre-dose and up to 10 hours post-dose in each treatment period. The washout period between the treatment arms was 7 days. The pharmacokinetic results are presented below.

| Table 1. Pharmacokinetic parameters of (S)-Ibuprofen (Mean ± SD, t_max, median, range) |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Treatment                        | AUC_0-t         | AUC_0-\infty    | C_max           | t_max           | T_1/2           |
|                                  | (ng/ml/h)       | (ng/ml/h)       | (ng/ml)         | (h)             | (h)             |
| Test (Ibuprofen)                 | 38086.2±7449.1  | 39476.5±8301.8  | 11280.0±2250.8  | 1.33 (0.333 -3.00) | 2.29±0.31 (13.36) |
| Reference1 (Nurofen Suspension)  | 36302.4±7572.7  | 37514.4±8250.7  | 9931.7±1914.5   | 1.00 (0.400 – 4.00) | 2.24±0.32 (14.36) |
| *Ratio (90% CI)                  | 105.1 (102.9-107.4)  | 105.4 (103.1-107.7) | 112.9 (105.8-120.5) |                 |                 |
| Reference2 (Nurofen Tablets)     | 37722.1±7372.9  | 39290.5±8307.8  | 9766.5±1470.0   | 1.50 (0.667 – 4.00) | 2.27±0.31 (13.83) |
| *Ratio (90% CI)                  | 101.0 (98.5-103.5)  | 100.6 (97.9-103.3) | 114.8 (107.74-122.3) |                 |                 |

AUC_0-\infty area under the plasma concentration-time curve from time zero to infinity
AUC_0-t area under the plasma concentration-time curve from time zero to t hours
C_max maximum plasma concentration
T_max time for maximum concentration
T_1/2 half-life

*ln-transformed values
Table 2. Pharmacokinetic parameters of (R)-Ibuprofen (Mean ± SD t_{max}, median, range)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>AUC_{0-t} (ng/ml/h)</th>
<th>AUC_{0-∞} (ng/ml/h)</th>
<th>C_{max} (ng/ml)</th>
<th>t_{max} (h)</th>
<th>T_{1/2} (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test (Ibuprofen)</td>
<td>31623.7±6362.9</td>
<td>32042.1±6342.8</td>
<td>11315.5±2349.5</td>
<td>1.33</td>
<td>1.63±0.26</td>
</tr>
<tr>
<td>Reference1 (Nurofen Suspension)</td>
<td>29475.7±8905.5</td>
<td>29914.3±8997.6</td>
<td>9835.0±2296.7</td>
<td>0.833</td>
<td>1.60±0.27</td>
</tr>
<tr>
<td>*Ratio (90% CI)</td>
<td>110.1 (104.7-115.8)</td>
<td>109.9 (104.5-115.67)</td>
<td>115.4 (107.6-123.7)</td>
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<tr>
<td>Reference2 (Nurofen Tablets)</td>
<td>31918.5±6223.5</td>
<td>32344.4±6591.0</td>
<td>10116.1±1956.5</td>
<td>1.33</td>
<td>1.61±0.0.25</td>
</tr>
<tr>
<td>*Ratio (90% CI)</td>
<td>99.1 (96.1-102.2)</td>
<td>99.1 (96.1-102.2)</td>
<td>111.9 (104.6-119.7)</td>
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</table>

*AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours
AUC_{0-∞} area under the plasma concentration-time curve from time zero to infinity
C_{max} maximum plasma concentration
t_{max} time for maximum concentration
T_{1/2} half-life

*In-transformed values

Bioequivalence Conclusion
The Guidance on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1) defines the 90% confidence limits as 80.00% to 125.00% for C_{max} and AUC values. The 90% confidence intervals of the test/reference ratio for AUC_{0-∞}, AUC_{0-t}, and C_{max} lie within the acceptable limits for ibuprofen. Thus, the data support the claim that the applicant’s test product (2 x 100 mg) is bioequivalent to the reference products Nurofen 100mg/5ml oral suspension (1 x 10ml; manufactured by Crookes Healthcare Limited, UK) and Nurofen 200 mg Tablet (1 x 200 mg tablet; manufactured by Crookes Healthcare Limited, UK), under fasting conditions.

Efficacy
The efficacy of ibuprofen is well-known. No new efficacy data have been submitted and none are required for this type of application.

Safety
With the exception of the safety data generated during the bioequivalence study, no new safety data were submitted and none are required for this type of application. No new or unexpected safety issues arose during the bioequivalence study.

Pharmacovigilance System and Risk Management Plan
The RMS considers that the Pharmacovigilance System, as described by the applicant, fulfils the requirements and 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 either in the Community or in a third country.

The applicant has provided an accepted Risk Management Plan (RMP).

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
The SmPC, PIL and labels are acceptable from a clinical perspective. The SmPC is consistent with that for the originator product. The PIL is consistent with the details in the SmPC and in line with current guidance. The labelling is in line with current guidance.
Clinical Expert Report (Clinical Overview)
The clinical overview has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

Conclusion
The grant of a Marketing Authorisation is recommended.

IV OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT
QUALITY
The important quality characteristics of Ibuprofen chewable capsules, soft 100 mg 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 were submitted. As the pharmacokinetics, pharmacodynamics and toxicology of ibuprofen are well-known, no additional data were required.

No new non-clinical data were submitted and none are required for this type of application.

EFFICACY
With the exception of the bioequivalence study, no new data were submitted and none are required for this type of application.

Bioequivalence has been demonstrated between the applicant’s test product and the reference products Nurofen 100mg/5ml oral suspension (1 x 10ml of a 100mg/5ml oral suspension; manufactured by Crookes Healthcare Limited, UK) and Nurofen 200 mg Tablet (1 x 200mg tablet; manufactured by Crookes Healthcare Limited, UK), under fasting conditions.

SAFETY
With the exception of the safety data from the bioequivalence study, no new data were submitted and none are required for this type of application. As the safety profile of ibuprofen is well known, no additional safety data were required. No new or unexpected safety concerns arose from the bioequivalence study.

PRODUCT LITERATURE
The SmPC, PIL and labelling text are satisfactory and consistent with those for the reference product, where appropriate and in line with current guidance.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with ibuprofen is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is therefore considered to be positive.
Module 6

STEPS TAKEN AFTER INITIAL THE PROCEDURE - SUMMARY

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