Celecoxib 100 mg capsules, hard
Celecoxib 200 mg capsules, hard

PL 35507/0133 and 0134

UKPAR

TABLE OF CONTENTS

Lay Summary .......................... Page 2
Scientific Discussion ................. Page 4
Steps Taken for Assessment ......... Page 12
Summary of Product Characteristics Page 13
Patient Information Leaflet .......... Page 14
Labelling .............................. Page 15
LAY SUMMARY

Celecoxib 100 mg and 200 mg capsules, hard

This is a summary of the Public Assessment Report (PAR) for Celecoxib 100 mg capsules, hard (PL 35507/0133) and Celecoxib 200 mg capsules, hard (PL 35507/0134). It explains how Celecoxib 100 mg and 200 mg capsules, hard, 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 Celecoxib 100 mg and 200 mg capsules, hard.

The products will be referred to as Celecoxib 100 mg and 200 mg capsules throughout the remainder of this report.

For practical information about using Celecoxib 100 mg and 200 mg capsules patients should read the package leaflet or contact their doctor or pharmacist.

What are Celecoxib 100 mg and 200 mg capsules, and what are they used for?

Celecoxib 100 mg and 200 mg capsules contain the active ingredient celecoxib. They are used for the relief of signs and symptoms of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis in adults.

This medicine is for use in adult patients only.

This medicine is identical to Bixocel 100 mg and 200 mg capsules, hard (PL 14048/0224 and 0225) which were granted Marketing Authorisations in the UK on 31 January 2014.

How are Celecoxib 100 mg and 200 mg capsules used?

The patient should always take this medicine exactly as their doctor has told them. The patient must check with their doctor or pharmacist if they are not sure. If the patient thinks or feels that the effect of celecoxib is too strong or too weak, they should talk to their doctor or pharmacist. The patient’s doctor will tell the patient what dose they should take. As the risk of side effects associated with heart problems may increase with dose and duration of use, it is important that the patient uses the lowest dose that controls their pain and they should not take celecoxib for longer than necessary to control symptoms.

The dose advised for treatment and its duration will depend on the reason why this medicine has been prescribed.

This medicine should be swallowed whole with a drink of water. The capsules can be taken at any time of the day with or without food. However, the patient should try to take each dose of celecoxib at the same time each day.

The patient should contact their doctor within two weeks of starting treatment if they do not experience any benefit.

Suddenly stopping treatment with celecoxib, may lead to the patient’s symptoms getting worse. The patient must not stop taking celecoxib unless their doctor tells them to. The patient’s doctor may tell the patient to reduce the dose over a few days before stopping completely.

Celecoxib 100 mg and 200 mg capsules can be obtained only with a prescription.

For further information on how Celecoxib 100 mg and 200 mg capsules are used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.
How do Celecoxib 100 mg and 200 mg capsules work?
Celecoxib belongs to a group of medicinal products called nonsteroidal anti-inflammatory drugs (NSAID), and specifically a sub-group known as (COX-2) inhibitors. The human body makes prostaglandins that may cause pain and inflammation. In conditions such as rheumatoid arthritis and osteoarthritis the body makes more of these. Celecoxib acts by reducing the production of prostaglandins, thereby reducing the pain and inflammation.

What benefits of Celecoxib 100 mg and 200 mg capsules have been shown in studies?
The applications for Celecoxib 100 mg and 200 mg capsules are considered to be identical to the previously authorised applications for Bixocel 100 mg and 200 mg capsules, hard (PL 14048/0224 and 0225), with the same benefits and risks. So, no new studies have been provided for Celecoxib 100 mg and 200 mg capsules; however, reference is made to the studies for Bixocel 100 mg and 200 mg capsules, hard (PL 14048/0224 and 0225).

The company (Lupin (Europe) Limited) referred to data provided by Synthon BV for the grant of licences for Bixocel 100 mg and 200 mg capsules, hard (PL 14048/0224 and 0225) as a basis for the grant of identical licences for Celecoxib 100 mg and 200 mg capsules (PL 35507/0133-0134).

What are the possible side effects from Celecoxib 100 mg and 200 mg capsules?
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Celecoxib 100 mg and 200 mg capsules are considered to be identical to the previously authorised applications for Bixocel 100 mg and 200 mg capsules, hard (PL 14048/0224 and 0225) with the same benefits and risks.

For a full list of all the side effects reported with Celecoxib 100 mg and 200 mg capsules see section 4 of the package leaflet, available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

Why are Celecoxib 100 mg and 200 mg capsules approved?
No new or unexpected safety concerns arose from these applications. The MHRA, therefore, considered that the benefits of Celecoxib 100 mg and 200 mg capsules outweigh their risks; and the grant of Marketing Authorisations (licences) was recommended.

What measures are being taken to ensure the safe and effective use of Celecoxib 100 mg and 200 mg capsules?
A Risk Management Plan has been developed to ensure that Celecoxib 100 mg and 200 mg capsules are 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 Celecoxib 100 mg and 200 mg capsules 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 Celecoxib 100 mg and 200 mg capsules
Marketing Authorisations were granted in the UK on 03 November 2014.

The full PAR for Celecoxib 100 mg and 200 mg capsules follows this summary.

For more information about treatment with Celecoxib 100 mg and 200 mg capsules read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in November 2014.
Celecoxib 100 mg capsules
Celecoxib 200 mg capsules

PL 35507/0133 and 0134

UKPAR

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>5</td>
</tr>
<tr>
<td>Pharmaceutical assessment</td>
<td>6</td>
</tr>
<tr>
<td>Non-clinical assessment</td>
<td>9</td>
</tr>
<tr>
<td>Clinical assessment</td>
<td>10</td>
</tr>
<tr>
<td>Overall conclusion and benefit/risk assessment</td>
<td>11</td>
</tr>
</tbody>
</table>
INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Lupin (Europe) Limited Marketing Authorisations for the medicinal products Celecoxib 100 mg and 200 mg capsules (PL 35507/0133 and 0134) on 03 November 2014. The products are prescription-only medicines (POM) indicated in adults for symptomatic relief in the treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis.

These applications were submitted as abridged applications according to Article 10c of Directive 2001/83/EC, as amended.

The applications for Celecoxib 100 mg and 200 mg capsules cross-refer to Bixocel 100 mg and 200 mg capsules, hard (PL 14048/0224 and 0225) which were authorised to Synthon BV, Netherlands on 31 January 2014. The latter products were authorised following an incoming Decentralised Procedure (NL/H/2796/01-02/DC) submitted under Article 10(1) of directive 2001/83/EC, as amended, applicable for a generic product, cross-referring to the innovator products Celebra 100 mg and 200 mg capsules, hard, authorised to Pfizer AB in Sweden on 03 December 1999 (Swedish Marketing Authorisation numbers 14838 and 14839).

Celecoxib is an oral, selective, cyclooxygenase-2 (COX-2) inhibitor within the clinical dose range (200-400 mg daily). No statistically significant inhibition of COX-1 (assessed as \textit{ex vivo} inhibition of thromboxane B$_2$ [TxB$_2$] formation) was observed in this dose range in healthy volunteers.

Cyclooxygenase is responsible for generation of prostaglandins. Two isoforms, COX-1 and COX-2, have been identified. COX-2 is the isoform of the enzyme that has been shown to be induced by pro-inflammatory stimuli and has been postulated to be primarily responsible for the synthesis of prostanoid mediators of pain, inflammation, and fever. COX-2 is also involved in ovulation, implantation and closure of the ductus arteriosus, regulation of renal function, and central nervous system functions (fever induction, pain perception and cognitive function). It may also play a role in ulcer healing. COX-2 has been identified in tissue around gastric ulcers in man but its relevance to ulcer healing has not been established.

The difference in antiplatelet activity between some COX-1 inhibiting NSAIDs and COX-2 selective inhibitors may be of clinical significance in patients at risk of thrombo-embolic reactions. COX-2 selective inhibitors reduce the formation of systemic (and therefore possibly endothelial) prostacyclin without affecting platelet thromboxane.

Celecoxib is a diaryl-substituted pyrazole, chemically similar to other non-arylamine sulfonamides (e.g. thiazides, furosemide) but differs from arylamine sulfonamides (e.g. sulfamethoxizole and other sulfonamide antibiotics).

No new data were submitted nor were necessary to be submitted for these applications, as the data are identical to those of the previously granted cross-reference products.
PHARMACEUTICAL ASSESSMENT

1. INTRODUCTION
These are abridged applications for Celecoxib 100 mg and 200 mg capsules (PL 35507/0133 and 0134) submitted under Article 10c of Directive 2001/83/EC, as amended.

The applications cross-refer to Bixocel 100 mg and 200 mg capsules, hard (PL 14048/0224 and 0225) which were authorised to Synthon BV, Netherlands on 31 January 2014.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1 Name
The proposed names of the products are Celecoxib 100 mg and 200 mg capsules. The products have been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
Each capsule for oral use contains 100 mg or 200 mg of celecoxib.

Both capsule strengths (100 mg and 200 mg) of the finished product are packed into polyvinyl chloride (PVC)/aluminium blister strips containing 1, 10, 20, 30, 40, 50, 60 and 100 capsules in a carton box.

Not all pack sizes may be marketed.

The proposed shelf life is 30 months with no special storage conditions.

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

2.3 Legal status
On approval, the products will be available as prescription-only medicines (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company
Lupin (Europe) Limited, Victoria Court, Bexton Road, Knutsford, Cheshire, WA16 0PF, UK.

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

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

2.6 Qualitative and quantitative composition
The proposed compositions are consistent with the details registered for the cross-reference products.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference products and the maximum batch sizes are stated.
2.8 Finished product/shelf-life specification
The proposed finished product specifications are in line with the details registered for the cross-reference products.

2.9 Drug substance specification
The proposed drug substance specifications are consistent with the details registered for the cross-reference products.

2.10 TSE Compliance
With the exception of lactose monohydrate and gelatin, none of the excipients contain materials of animal or human origin. The supplier of lactose monohydrate has confirmed that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that intended for human consumption. In addition, the supplier has confirmed that no ruminant material of any kind is used during the production of lactose monohydrate. 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 minimising of risk of transmission of Bovine Spongiform Encephalopathy/Transmissible Spongiform Encephalopathies (BSE/TSE). This is consistent with the cross-reference products.

2.11 Bioequivalence
No bioequivalence data are required to support these applications because the proposed products are manufactured to the same formula utilising the same processes as the cross-reference products, Bixocel 100 mg and 200 mg capsules, hard (PL 14048/0224 and 0225).

3. EXPERT REPORT
The applicant cross-refers to the data for Bixocel 100 mg and 200 mg capsules, hard (PL 14048/0224 and 0225) to which these applications are claimed to be identical. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See Section 2.1 for details of the proposed product names. The appearance of each product is identical to that of the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPCs)
The proposed Summaries of Product Characteristics are consistent with the details registered for the cross-reference products.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
PIL
The Patient Information Leaflet has been prepared in line with the details registered for the cross-reference products.

User-testing of the PIL for Celecoxib 100 mg and 200 mg capsules has been accepted based on the bridging report provided by the applicant making reference to the successful user-testing of the PIL for to Bixocel 100 mg and 200 mg capsules, hard (PL 14048/0224 and 0225) as the ‘parent PIL’.

Carton and label
The proposed artwork is consistent with the artwork registered for the cross-reference products and complies with statutory requirements. In line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSION
The data submitted with the applications are acceptable. The grant of Marketing Authorisations is recommended.
NON-CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the applications are identical versions of already authorised products, it is not expected that environmental exposure will increase following approval of the Marketing Authorisations for the proposed products.

The grant of Marketing Authorisations is recommended.
CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

An acceptable Risk Management Plan (RMP) has been submitted.

The grant of Marketing Authorisations is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for these applications are consistent with those previously assessed for the cross-reference products and as such have been judged to be satisfactory.

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

EFFICACY
These applications are identical to the previously granted applications for Bixocel 100 mg and 200 mg capsules, hard (PL 14048/0224 and 0225).

SAFETY
No new safety data were supplied or required for these applications. Celecoxib has a well-established safety profile. No new or unexpected safety concerns arose from these applications.

PRODUCT LITERATURE
The SmPCs, PIL and labelling are satisfactory, and consistent with those for the cross-reference products.

BENEFIT/RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference products. Extensive clinical experience with celecoxib is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is, therefore, considered to be positive.
Celecoxib 100 mg capsules
Celecoxib 200 mg capsules

PL 35507/0133 and 0134

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Marketing Authorisation applications on 09 May 2014.
2 Following standard checks and communication with the applicant the MHRA considered the application valid on 14 May 2014.
3 Following assessment of the applications the MHRA requested further information relating to the dossier on 12 August 2014.
4 The applicant responded to the MHRA’s request, providing further information on the 19 September 2014
5 The applications were granted on 03 November 2014.
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.
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.