Public Assessment Report

UKPAR

Montelukast 10mg film-coated tablets

(Montelukast sodium)

UK Licence No: PL 20416/0547

Crescent Pharma Limited.
LAY SUMMARY

Montelukast 10mg film-coated tablets
(montelukast sodium)

This is a summary of the Public Assessment Report (PAR) for Montelukast 10mg film-coated tablets (PL 20416/0547). It explains how Montelukast 10mg film-coated tablets 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 Montelukast 10mg film-coated tablets.

For practical information about using Montelukast 10mg film-coated tablets patients should read the package leaflet or contact their doctor or pharmacist.

This product will be referred to as Montelukast tablets throughout the remainder of this public assessment report (PAR).

What are Montelukast tablets and what are they used for?
This medicine is used to treat asthma, preventing asthma symptoms during the day and night.

Montelukast tablets are used for the treatment of patients aged 15 years and older who are not adequately controlled on their medication and need additional therapy.

Montelukast tablets also help prevent the narrowing of airways triggered by exercise. In those asthmatic patients in whom Montelukast tablets are indicated in asthma, this medicine can also provide symptomatic relief of seasonal allergic rhinitis.

The patient’s doctor will determine how this should be used depending on the symptoms and severity of the patient’s asthma.

This application is the same as Montelukast 10 mg film-coated tablets (PL 42831/0001) which is already authorised.

The company (Warren Generics s.r.o.) that makes Montelukast 10 mg film-coated tablets (PL 42831/0001) has agreed that its scientific data can be used as a basis for the grant of an identical licence for Montelukast tablets.

How do Montelukast tablets work?
This medicine contains the active ingredient montelukast sodium which is a leukotriene receptor antagonist that blocks substances called leukotrienes. Leukotrienes cause narrowing and swelling of airways in the lungs and also cause allergy symptoms. By blocking leukotrienes, montelukast improves asthma symptoms, helps control asthma and improves seasonal allergy symptoms (also known as hay fever or seasonal allergic rhinitis).

How are Montelukast tablets used?
The pharmaceutical form of this medicine is a film-coated tablet and the route of administration is oral (by mouth).

The patient should always use this medicine exactly as their doctor has told them. The patient should check with their doctor if they are not sure.
The recommended dose is one 10mg tablet once a day. The tablet should be taken even when the patient has no symptoms or has an acute asthma attack.

**Use in adults and adolescent 15 years of age and older**
The recommended dose is one 10mg tablet to be taken daily in the evening. Montelukast tablets may be taken with or without food.

**Use in children and adolescents younger than 15 years**
This product is not suitable for children and adolescents under 15 years of age for whom alternative products available in lower strengths are recommended.

If the patient is taking Montelukast tablets, they must be sure that they do not take any other products that contain the same active ingredient, montelukast.

This medicine can only be obtained with a prescription.

For further information on how Montelukast tablets are used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

**What benefits of Montelukast tablets have been shown in studies?**
Montelukast tablets is considered identical to previously authorised Montelukast 10 mg film-coated tablets (PL 42831/0001) with the same benefits and risks. So, no new studies have been provided for Montelukast tablets, but reference is made to the studies for Montelukast 10 mg film-coated tablets (PL 42831/0001).

**What are the possible side effects from Montelukast tablets?**
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Montelukast tablets is considered to be identical to the previously authorised application for Montelukast 10 mg film-coated tablets (PL 42831/0001) with the same benefits and risks.

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

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

**Why was Montelukast tablets approved?**
The MHRA decided that the benefits of Montelukast tablets are greater than the risks and recommended that they are approved for use.

**What measures are being taken to ensure the safe and effective use of Montelukast tablets?**
A Risk Management Plan has been developed to ensure that Montelukast tablets 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 Montelukast 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/healthcare professionals will be monitored/reviewed continuously.
Other information about Montelukast tablets
A Marketing Authorisation were granted in the UK on 27 March 2018.

The full PAR for Montelukast tablets follows this summary.

For more information about treatment with Montelukast tablets read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in May 2018.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Introduction</td>
<td>6</td>
</tr>
<tr>
<td>II Quality aspects</td>
<td>7</td>
</tr>
<tr>
<td>III Non-clinical aspects</td>
<td>9</td>
</tr>
<tr>
<td>IV Clinical aspects</td>
<td>9</td>
</tr>
<tr>
<td>V User consultation</td>
<td>10</td>
</tr>
<tr>
<td>VI Overall conclusion, benefit/risk assessment and recommendation</td>
<td>10</td>
</tr>
<tr>
<td>Table of content of the PAR update</td>
<td>14</td>
</tr>
</tbody>
</table>
I INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Crescent Pharma Limited a Marketing Authorisation for the medicinal product Montelukast tablets (PL 20416/0547) on 27 March 2018.

This product is a prescription only medicine (POM) and is indicated in the treatment of asthma as add-on therapy in adolescent of 15 years of age and older and adults with mild to moderate persistent asthma who are inadequately controlled on inhaled corticosteroids and in whom “as-needed” short acting β-agonists provide inadequate clinical control of asthma. In those asthmatic patients in whom montelukast is indicated in asthma, it can also provide symptomatic relief of seasonal allergic rhinitis.

Montelukast tablets are also indicated in the prophylaxis of asthma in which the predominant component is exercise-induced bronchoconstriction.

Montelukast is indicated in adults and adolescents from the age of 15 years.

This application was submitted as a simple abridged (informed consent) application according to Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to the medicinal product Montelukast 10 mg film-coated tablets which was first authorised to the marketing authorisation holder (MAH) Warren Generics s.r.o (PL 42831/0001) on 03 March 2015.

The cysteinyleukotrienes (LTC4, LTD4, LTE4) are potent inflammatory eicosanoids released from various cells including mast cells and eosinophils. These important pro-asthmatic mediators bind to cysteinyl leukotriene (CysLT) receptors. The CysLT type-1 (CysLT₁) receptor is found in the human airway (including airway smooth muscle cells and airway macrophages) and on other proinflammatory cells (including eosinophils and certain myeloid stem cells). CysLTs have been correlated with the pathophysiology of asthma and allergic rhinitis. In asthma, leukotriene-mediated effects include bronchoconstriction, mucous secretion, vascular permeability, and eosinophil recruitment. In allergic rhinitis, CysLTs are released from the nasal mucosa after allergen exposure during both early- and late-phase reactions and are associated with symptoms of allergic rhinitis. Intranasal challenge with CysLTs has been shown to increase nasal airway resistance and symptoms of nasal obstruction.

Montelukast is an orally active compound which binds with high affinity and selectivity to the CysLT₁ receptor. In clinical studies, montelukast inhibits bronchoconstriction due to inhaled LTD4 at doses as low as 5mg. Bronchodilation was observed within 2 hours of oral administration. The bronchodilation effect caused by a β-agonist was additive to that caused by montelukast. Treatment with montelukast inhibited both early- and late-phase bronchoconstriction due to antigen challenge. Montelukast, compared with placebo, decreased peripheral blood eosinophils in adult and paediatric patients. In a separate study, treatment with montelukast significantly decreased eosinophils in the airways (as measured in sputum) and in peripheral blood while improving clinical asthma control.

No new data were submitted nor were necessary to be submitted for this application, as the data are identical to the data for the previously granted cross-referenced 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.
II QUALITY ASPECTS

II.1 Introduction
This is an abridged application for Montelukast tablets (PL 20416/0547) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to the medicinal product Montelukast 10 mg film-coated tablets which was first authorised to the marketing authorisation holder (MAH) Warren Generics s.r.o (PL 42831/0001) on 03 March 2015. The application is considered valid.

II.2 Drug Substance
Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

II.3 Medicinal Product
Name
The proposed product name for this application is Montelukast 10mg film-coated tablets. The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes
Each film-coated tablet contains montelukast sodium equivalent to 10mg montelukast. The finished product is packaged into OPA-Al-PVC/Al blisters in a pack size of 28 tablets.

The proposed shelf life of the unopened product is 30 months with the storage conditions ‘Do not store above 30°C, store in the original package in order to protect from moisture and light.’

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

Legal status
Prescription only medicine (POM).

Marketing Authorisation Holder/Contact Persons/Company
Crescent Pharma Limited, Units 3 & 4, Quidhampton Business Units, Polhampton Lane, Overton, Hampshire RG25 3ED, UK.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory 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 processes are consistent with the details registered for the cross-reference product and the maximum batch size is stated.
Finished product/shelf-life specification
The proposed finished product specification is in line with the details registered for the cross-reference products.

TSE Compliance
With the exception of lactose monohydrate none of the excipients used contain material of animal or human origin. The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption.

Bioequivalence
No bioequivalence data are required to support this simple abridged application because the proposed product is manufactured to the same formula utilising the same processes as the cross-reference product, Montelukast 10 mg film-coated tablets (PL 42831/0001).

Expert Report
The applicant cross-refers to the data for Montelukast 10 mg film-coated tablets (PL 42831/0001) to which this application is claimed to be identical. This is acceptable.

Product Name and Appearance
See Section II.3 ‘Medicinal Product; Name’ for details of the proposed product name. The appearance of the product is identical to that of the cross-reference product.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The data submitted with this application is acceptable. The grant of a Marketing Authorisation is recommended.
III NON-CLINICAL ASPECTS

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

Ecotoxicity/environmental risk assessment (ERA)
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

Discussion on the non-clinical aspects
The grant of a Marketing Authorisation is recommended.

IV CLINICAL ASPECTS

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

Risk Management Plan (RMP)
The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterize, prevent or minimise risks relating to Montelukast tablets.

A summary of safety concerns and planned risk minimisation activities, as approved in the RMP are listed below:

<table>
<thead>
<tr>
<th>Summary of safety concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Important identified risks</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Important potential risks</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Missing information</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Routine pharmacovigilance and routine risk minimisation are proposed for all safety concerns.
Discussion on the clinical aspects
The grant of a Marketing Authorisation is recommended.

V User consultation
A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to the PIL for Montelukast 10 mg film-coated tablets (Warren Generics s.r.o). 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 safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with montelukast sodium is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is, therefore, considered to be positive.
Summaries of Product Characteristics (SmPC), Patient Information Leaflets (PIL) and Labels

The SmPC and PIL are consistent with the details registered for the cross-reference products.

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

The approved labelling for this medicine is presented below:
Montelukast 10mg Film-coated tablets

Read the package leaflet before use.
Do not store above 30°C.
Store in the original package in order to protect from moisture and light.
One film-coated tablet contains montelukast sodium, which is equivalent to 10mg montelukast.
Also contains lactose.
### Annex 1

**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, commitments)

<table>
<thead>
<tr>
<th>Scope</th>
<th>Procedure number</th>
<th>Product information affected</th>
<th>Date of start of the procedure</th>
<th>Date of end of procedure</th>
<th>Approval/ non approval</th>
<th>Assessment report attached Y/N (version)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>