Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

UKPAR

Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets

(Olmesartan medoxomil)

UK Licence No: PL 20416/0540-42

Crescent Pharma Limited

LAY SUMMARY
Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (Olmesartan medoxomil)

This is a summary of the Public Assessment Report (PAR) for Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (PL 20416/0540-42). For ease of reading, these medicinal products will be referred to as Olmesartan medoxomil Tablets in this Lay Summary.

This summary explains how Olmesartan medoxomil Tablets 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 these products.

For practical information about using Olmesartan medoxomil Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Olmesartan medoxomil Tablets and what are they used for?
This medicine is the same as Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (PL 19156/0097-9; Jubilant Pharmaceuticals NV), which are already authorised in the UK. The licence holder (Jubilant Pharmaceuticals NV) for Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (PL 19156/0097-9) has agreed that its own scientific data can be used as a basis for the grant of identical licences for Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (PL 20416/0540-42).

Olmesartan medoxomil tablets are used for the treatment of high blood pressure (also known as 'hypertension') in adults and in children and adolescents aged 6 to less than 18 years. High blood pressure can damage blood vessels in organs such as the heart, kidneys, brain and eyes. In some cases may lead to a heart attack, heart or kidney failure, stroke or blindness. Usually high blood pressure has no symptoms. It is important to have the blood pressure checked to prevent damage occurring.

How do Olmesartan medoxomil Tablets work?
Olmesartan medoxomil tablets contain the active ingredient olmesartan medoxomil, which belongs to a group of medicines called angiotensin-II receptor antagonists. This medicine lowers blood pressure by relaxing the blood vessels.

How are Olmesartan medoxomil Tablets used?
Olmesartan medoxomil tablets are taken orally with or without food. The whole tablet must be swallowed with a sufficient amount of water (e.g. one glass). The tablets should not be chewed. If possible, take your daily dose at the same time each day, for example at breakfast time.

The recommended starting dose is one 10mg tablet once a day. However, if the blood pressure is not controlled, a doctor may decide to change the dose up to 20mg or a maximum of 40mg once a day, or prescribe additional medicines.

In patients with mild to moderate kidney disease, the dose will not be higher than 20mg once a day.

This medicine can only be obtained with a prescription.

For further information on how Olmesartan medoxomil Tablets are used, please see the Summaries of Product Characteristics or the package leaflet available on the MHRA website.

What benefits of Olmesartan medoxomil Tablets have been shown in studies?
As Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (PL 20416/0540-42) are considered to be identical to the reference products, Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (PL 19156/0097-9), their benefits and risks are taken as being the same as those for the reference products.

What are the possible side effects from Olmesartan medoxomil Tablets?
Like all medicines, Olmesartan medoxomil Tablets can cause side effects, although not everybody gets them.

For the full list of all side effects reported with Olmesartan medoxomil Tablets, see section 4 of the package leaflet.

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

Why are Olmesartan medoxomil Tablets approved?
No new or unexpected safety concerns arose from these applications. It was, therefore, considered that the benefits of Olmesartan medoxomil Tablets outweigh the risks, and the grant of Marketing Authorisations was recommended.

What measures are being taken to ensure the safe and effective use of Olmesartan medoxomil Tablets?
A risk management plan (RMP) has been developed to ensure that Olmesartan medoxomil Tablets are used as safely as possible. Based on this plan, safety information has been included in the Summaries of Product Characteristics and the patient information leaflet for Olmesartan medoxomil 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 and reviewed continuously.

Other information about Olmesartan medoxomil Tablets
Marketing Authorisations were granted in the UK on 05 September 2018.

The full PAR for Olmesartan medoxomil Tablets follows this summary.

This summary was last updated in October 2018.

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I INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Crescent Pharma Limited Marketing Authorisations for the medicinal products Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (PL 20416/0540-42) on 05 September 2018.

These are prescription only medicines (POM), used for the treatment of essential hypertension in children and adolescents from 6 to less than 18 years of age.

These applications were submitted as abridged simple applications, according to Article 10c of Directive 2001/83/EC, as amended. The applicant has cross-referred to Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets, which were originally authorised to Jubilant Pharmaceuticals NV (PL 19156/0097-9) on 02 July 2015.

Olmesartan medoxomil is a potent, orally active, selective angiotensin II receptor (type AT_1) antagonist. It is expected to block all actions of angiotensin II mediated by the AT_1 receptor, regardless of the source or route of synthesis of angiotensin II. The selective antagonism of the angiotensin II (AT_1) receptors results in increases in plasma renin levels and angiotensin I and II concentrations, and some decrease in plasma aldosterone concentrations.
Angiotensin II is the primary vasoactive hormone of the renin-angiotensin-aldosterone system and plays a significant role in the pathophysiology of hypertension via the type 1 (AT_1) receptor.

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

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 these product.

II QUALITY ASPECTS

II.1 Introduction

These are simple (informed consent) applications for Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (PL 20416/0540-42), submitted under Article 10c of Directive 2001/83/EC, as amended. The applicant has cross-referred to Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets, which were originally authorised to Jubilant Pharmaceuticals NV (PL 19156/0097-9) on 05 September 2018. The current applications are considered valid.

II.2. Drug Substance

Drug substance specification

The proposed drug substance specification is consistent with the details registered for the cross-reference products.

II.3. Medicinal Product

Name

The proposed product names are Olmesartan medoxomil 10, 20 and 40 mg Film coated-tablets. The products have been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack size

Each tablet contains 10 mg, 20 mg or 40 mg of olmesartan medoxomil, as active ingredient. The route of administration is oral.

The finished products are packed in laminated oriented polyamide (OPA)/aluminium/polyvinylchloride (PVC)-aluminium blister pack containing 28 film-coated tablets.

The proposed shelf-life is 2 years with a special storage condition “store below 25ºC”.

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

Marketing Authorisation Holder/Contact Persons/Company

Crescent Pharma Limited, Units 3 & 4, Quidhampton Business Units, Polhampton Lane, Overton, Hampshire RG25 3ED, United Kingdom

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

Manufacturer

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.

Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference products.

Manufacturing process

The proposed manufacturing process is consistent with the details registered for the cross-reference products and the maximum batch size is stated.

Finished product/shelf-life specification

The proposed finished product specifications are in line with the details registered for the cross-reference products.

Expert Report
The applicant cross-refers to the data for Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (PL 19156/0097-9), to which these applications are claimed to be identical. This is acceptable. The applicant has included expert reports of the applications. Signed declarations and copies of the experts' CVs are enclosed for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The quality data for these applications are consistent with those approved for Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (PL 19156/0097-9) and, as such, have been judged to be satisfactory. The grant of Marketing Authorisations is recommended.

III NON-CLINICAL ASPECTS

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

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

The grant of Marketing Authorisations is recommended.

IV CLINICAL ASPECTS

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

No bioequivalence data are required to support these simple abridged applications as the proposed products are manufactured to the same formula utilising the same process as the cross-reference products, Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (PL 19156/0097-9).

Risk Management Plan (RMP)
The Marketing Authorisation Holder (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, characterise, prevent or minimise risks relating to Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets.

A summary of safety concerns as approved in the RMP, is listed below:

Summary of safety concerns	
Important identified risks	• Hypersensitivity reactions • Symptomatic hypotension • Dual blockade of the renin-angiotensin-aldosterone system (RAAS) • Renal impairment (including renal failure) • Sprue-like enteropathy • Use in 2nd and 3rd trimester of pregnancy • Drug interaction with lithium • Hyperkalaemia
Important potential risks	• Rhabdomyolysis • Cardiovascular risks in patients with type 2 diabetes
Missing information	• Use in patients with severe hepatic impairment • Use in patients with severe renal impairment or recent kidney transplant • Use during breast-feeding • Use in paediatric population

Discussion on the clinical aspects
The grant of Marketing Authorisations is recommended for these applications.

V User consultation

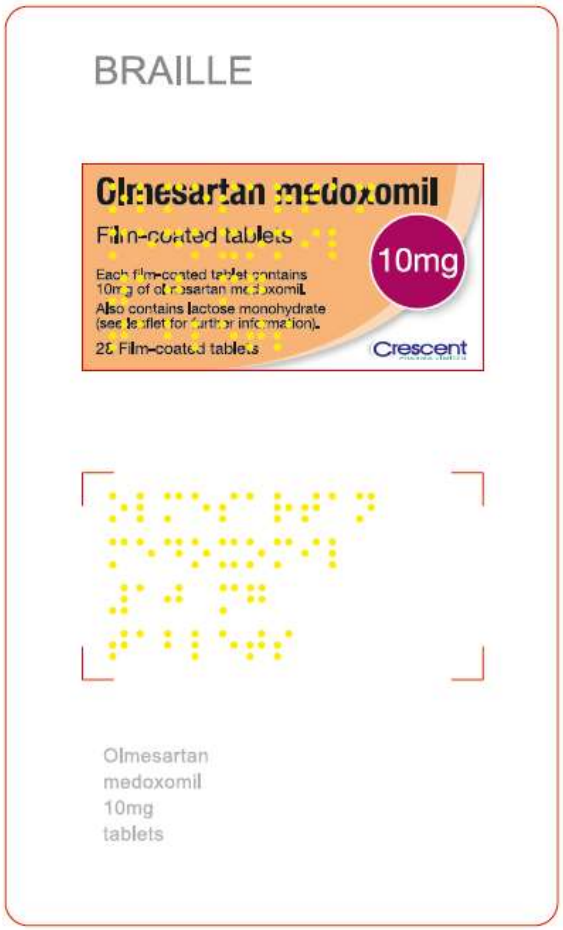
User testing of the package leaflet has been accepted, based on bridging reports provided by the applicant making reference to the user-testing of the PIL for Olmesartan medoxomil 10, 20 and 40 mg Film-coated tablets (Jubilant Pharmaceuticals NV). The products are from the same therapeutic class and have similar indications. A critical analysis demonstrated that the key messages for safe and effective use for both leaflets were similar. The justification on the rationale for bridging is accepted.

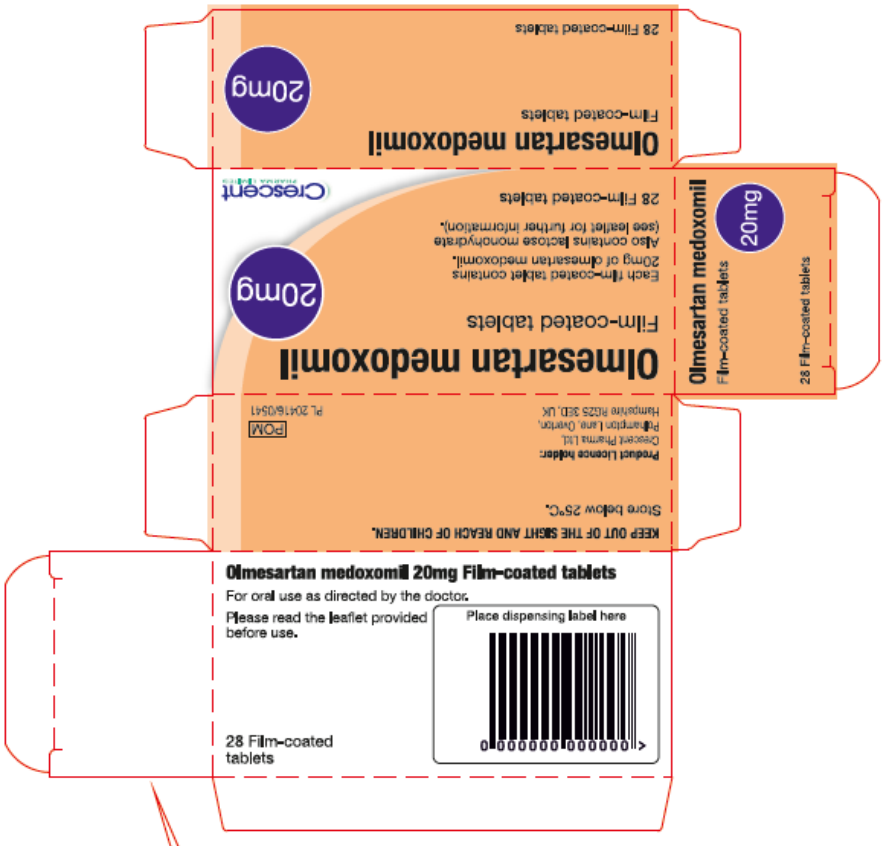
VI Overall conclusion, benefit/risk assessment and recommendation

The quality of the products is acceptable, and no new non-clinical or clinical concerns have been identified. The applicant's product is identical to the reference product. Extensive clinical experience with olmesartan medoxomil is considered to have demonstrated the therapeutic value of the compound. The benefit-risk assessment is, therefore, considered to be positive.

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

The approved labelling for Olmesartan medoxomil 10, 20 and 40 mg Film coated-tablets (PL 20416/0540-42) is presented below:


BRAILLE
Olmesartan medoxomil
Film-coated tablets
10mg
Each film-coated tablet contains 10mg of olmesartan medoxomil.
Also contains lactose monohydrate (see leaflet for further information).
28 Film-coated tablets
Crescent
Olmesartan medoxomil 10mg tablets


Olmesartan medoxomil
Film-coated tablets
20mg
28 Film-coated tablets
Olmesartan medoxomil 20mg Film-coated tablets
For oral use as directed by the doctor.
Please read the leaflet provided before use.
Place dispensing label here
28 Film-coated tablets
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.
Store below 25°C.
POM
PL 20416/0541


Crescent Pharma Ltd
OLMESARTAN MEDOXOMIL 20mg Tablets
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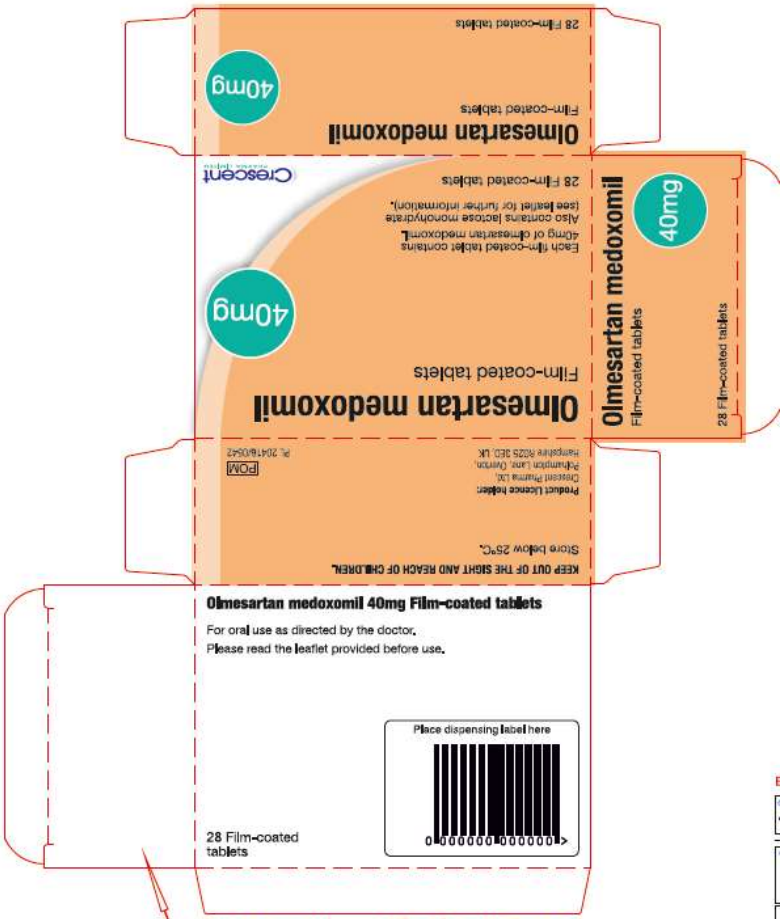
Olmesartan medoxomil
Film-coated tablets
40mg
28 Film-coated tablets
Olmesartan medoxomil 40mg Film-coated tablets
For oral use as directed by the doctor.
Please read the leaflet provided before use.
Place dispensing label here
28 Film-coated tablets
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.
Store below 25°C.
POM


Crescent Pharma Ltd
OLMESARTAN MEDOXOMIL 40mg Tablets
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BRAILLE
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Film-coated tablets
40mg
Each film-coated tablet contains 40mg of olmesartan medoxomil.
Also contains lactose monohydrate (see leaflet for further information).
28 Film-coated tablets
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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, commitmen

Date submitted	Application type	Scope	Outcome