IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Telmisartan Rowa 20 mg tablets
Telmisartan
PA0074/078/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Telmisartan Rowa 20 mg, 40 mg and 80 mg tablets, from Rowa Pharmaceuticals Ltd on 6th March 2020 for:

Hypertension:
Treatment of essential hypertension in adults.

Cardiovascular prevention:
Reduction of cardiovascular morbidity in adults with:
• manifest atherothrombotic cardiovascular disease (history of coronary heart disease, stroke, or peripheral arterial disease) or
• type 2 diabetes mellitus with documented target organ damage.

This application for a marketing authorisation was submitted in accordance with Article 10(1) of Directive 2001/83/EC, as amended, as a new national generic application. Telmisartan Rowa 20 mg, 40 mg and 80 mg tablets are a generic of the reference product Micardis 20mg, 40mg and 80mg tablets from Boehringer Ingelheim International GmbH. Micardis 20mg, 40mg and 80mg tablets is a well-known medicinal product with a proven chemical-pharmaceutical quality.

These products are subject to prescription which may be renewed, are for supply in pharmacies only and are for promotion to healthcare professionals only.

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA's website at www.hpra.ie .

Name of the product	Telmisartan Rowa 20/40/80 mg Tablet
Name(s) of the active substance(s) (INN)	TELMISARTAN
Pharmacotherapeutic classification (ATC code)	C09CA07
Pharmaceutical form and strength(s)	20 mg/40 mg/80 mg
Marketing Authorisation Number(s) in Ireland (PA)	PA0074/078/001-003
Marketing Authorisation Holder	Rowa Pharmaceuticals Limited

II. QUALITY ASPECTS

II.1. Introduction

This application is for Telmisartan Rowa 20 mg, 40 mg and 80 mg tablets.

II.2. Drug substance

The active substance is telmisartan, an established active substance described in theEuropean Pharmacopoeia, and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3. Medicinal product

P.1 Composition
The excipients in the medicinal product are listed in section 6.1 of the SmPC.
A visual description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development
The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

P.3 Manufacture of the Product
The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process has been validated according to relevant European and ICH guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients)
All ingredients comply with Ph. Eur. or are adequately controlled by the manufacturer's specifications.

P.5 Control of Finished Product
The Finished Product Specification is based on the pharmacopoeial monograph for tablets, and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site(s) have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material
The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the packaging complies with Ph. Eur. and EU legislation for use with foodstuffs requirements.

P.7 Stability of the Finished Product
Stability data on the finished product inthe proposed packaging have been provided in accordance with EU guidelines andsupport the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

II.4 Discussion on Chemical, Pharmaceuticaland Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of Telmisartan Rowa 20 mg, 40 mg and 80 mg tablets.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is the same as that present in Mirpresoc 20mg, 40mg and 80 mg tablets on the European market. No new preclinical data have been submitted. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application.

III.2 Pharmacology

See clinical section.

III.3 Pharmacokinetics

See clinical section.

III.4 Toxicology

Not applicable as this is an informed consent application.

III.5 Ecotoxicity/environmental risk assessment

Not applicable as this is an informed consent application.

III.6 Discussion on the non-clinical aspects

As this is an informed consent application, additional non-clinical data is not necessary for this application. The active substance telmisartan is well-known and its preclinical effects are well documented. Relevant preclinical aspects are outlined in section 5.3 of the SmPC.

IV. CLINICAL ASPECTS

IV.1 Introduction

Telmisartan is a well-known active substance with established efficacy and tolerability.

The content of the SmPCs approved during the national procedure are in accordance with those accepted for the reference products Micardis2 0mg, 40mg and 80mg tablets.

IV.2 Pharmacokinetics

Absorption:
Absorption of telmisartan is rapid although the amount absorbed varies. The mean absolute bioavailability for telmisartan is about 50 %. By 3 hours after administration plasma concentrations are similar whether telmisartan is taken fasting or with food.

Distribution:
Telmisartan is largely bound to plasmaprotein (> 99.5 %), mainly albumin and alpha-1 acid glycoprotein. The mean steady state apparent volume of distribution (Vdss) is approximately 500 l.

Biotransformation:
Telmisartan is metabolised by conjugation to the glucuronide of the parent compound. No pharmacological activity has been shown for the conjugate.

Elimination:
After oral administration telmisartan is nearly exclusively excreted with the faeces, mainly as unchanged compound. Cumulative urinary excretion is < 1% of dose.

IV.3 Pharmacodynamics

Telmisartan is an orally active and specific angiotensin II receptor (type AT1) antagonist.

IV.4 and IV.5 Clinical Efficacy and Safety

Telmisartan is a well-known active substance with established efficacy and tolerability. These medicinal products are the same as Micardis 20mg, 40mg and 80mg tablets on the European market.

The content of the SmPCs approved during the national procedure are in accordance with those accepted for the reference products Micardis 20mg, 40mg and 80mg tablets.

Pharmacovigilance System
The marketing authorisation holder (MAH) submitted a summary of the Pharmacovigilance System, including confirmation of the availability of an EU Qualified Person for Pharmacovigilance (EU-QPPV) and the means for notification of adverse reaction reports in the EU or from a Third Country.

Risk Management Plan

The Applicant submitted a Risk Management Plan to support this application. The following table outlines the summary of safety concerns:

Summary of safety concerns	
Important identified risks	• Renal dysfunction as a consequence of dual RAAS blockade • Sepsis • Foetotoxicity • Hypoglycaemia (in diabetic patients)
Important potential risks	• Increase of hepatic related adverse reactions in the Japanese population • Rhabdomyolysis • Malignancies
Missing information	NA

Routine risk minimisation measures and routine pharmacovigilance activities were proposed to address the safety concerns outlined above and this is considered acceptable.

The Applicant should submit Periodic Safety Update Reports (PSUR) Periodic Safety Update Reports (PSUR) in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

IV.6 Discussion on the clinical aspects

Telmisartan is a well-known substance and has been widely marketed. As this is an informed consent application no new efficacy or safety data have been submitted. Efficacy and safety is expected to be similar to the reference products Micardis 20mg, 40mg and 80mg tablets. The product information (SmPCs and Patient Leaflet) are identical to those of the reference products.

V. OVERALL CONCLUSIONS

Telmisartan Rowa 20mg, 40mg and 80 mg tablets are the same as Micardis 20mg, 40mg and 80mg tablets. Micardis 20mg, 40mg and 80mg tablets are well-known medicinal products with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

The HPRA, on the basis of the data submitted considered that Telmisartan Rowa 20mg, 40mg and 80 mg tablets (PA0074/078/001-003) were the same as the reference products and therefore granted a marketing authorisation for each strength.

VI. REVISION DATE

VII. UPDATES

This section reflects the significant changes following finalisation of the initial procedure.

SCOPE	**PROCEDURE NUMBER**	**PRODUCT INFORMATION AFFECTED**	**DATE OF START OF PROCEDURE**	**DATE OF END OF PROCEDURE**
