COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Telmisartan Glenmark 20 mg, 40 mg and 80 mg, film-coated tablets (telmisartan)

NL/H/4528/001-003/DC

Date: 27 February 2023

This module reflects the scientific discussion for the approval of Telmisartan Glenmark 20 mg, 40 mg and 80 mg, film-coated tablets. The procedure was finalised in the United Kingdom (UK/H/2633/001-003/DC). After a transfer in 2018, the current RMS is the Netherlands. The report presented below reflects the original procedure at the time of finalisation in the UK and has not been changed or updated since.

Safeguarding public health

MHRA

Public Assessment Report

Decentralised Procedure

Telmisartan Glenmark Generics/Telmisartan Glenmark 20, 40 and 80mg Film-coated Tablets

(Telmisartan)

UK/H/2633/001-3/DC
UK/H/4197-8/001-3/DC

UK licence no: PL 25258/0024-0026
PL 25258/0072 -0077

Applicant: Glenmark Generics (Europe) Limited

LAY SUMMARY

Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 Film-coated Tablets (Telmisartan)

This is a summary of the public assessment report (PAR) for Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets. This summary explains how Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated 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 Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets.

For practical information about Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets and what are they used for?

Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets are 'generic medicines'. This means that Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets are similar to 'reference medicines' already authorised in the European Union (EU) called Micardis 20 mg, 40 mg and 80 mg Film-coated Tablets. The active substance in this medicine is Telmisartan. Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets are used:

- in the treatment of essential hypertension (high blood pressure) in adults. Essential means that the high blood pressure is not caused by any other condition
- to reduce cardiovascular events (i.e. heart attack or stroke) in adults who are at risk because they have a reduced or blocked blood supply to the heart or legs, or have had a stroke or have high risk diabetes.

How are Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets used?

This is a prescription only medicine. Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets can be taken with or without food, but should be swallowed with some water or any other non-alcoholic drink. The recommended dose of this medicine is one tablet a day.

How do Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets work?

Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets belong to a class of medicines known as angiotensin II receptor antagonists. Angiotensin II is a substance produced in the body which causes the blood vessels to narrow, thus increasing the blood pressure. Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets work by blocking the effect of angiotensin II which causes the blood vessels to relax and therefore lowering the blood pressure.

How have Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets been studied?
Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets are generic medicines; studies in patients have been limited to tests to determine that they are bioequivalent to the reference medicines.
Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

What are the benefits and risks of Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets?
Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets are generic medicines and they are bioequivalent to the reference medicine. Therefore, the benefits and risks are taken as being the same as the reference medicine.

Why are Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets approved?
It was concluded that, in accordance with EU requirements, Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets have shown to have comparable quality and to be bioequivalent to the reference medicine; Micardis 20 mg, 40 mg and 80 mg Film-coated Tablets, therefore the view was that as for the reference medicine, the benefits outweigh the identified risks.

What measures are being taken to ensure the safe and effective use of Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets?
Safety information has been included in the Summary of Product Characteristics and the package leaflets for Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Telmisartan Glenmark Generics/ Telmisartan Glenmark 20mg, 40 mg and 80 mg Film-coated Tablets
Austria, Belgium, Bulgaria, Germany, Greece, Denmark, Finland, France, Ireland, Italy, Luxemburg, the Netherlands, Portugal, Spain , Sweden and the United Kindom agreed to grant Marketing Authorisations on 23 March 2011.

Marketing Authorisations were granted in the UK to Glenmark Pharmaceuticals Europe Limited on 19 April 2011.

The full PAR for Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets follows this summary. For more information about treatment with Telmisartan Glenmark Generics/ Telmisartan Glenmark 20 mg, 40 mg and 80 mg Film-coated Tablets, read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in June 2014

TABLE OF CONTENTS

Module 1
Information about initial procedure

Product Name	Telmisartan Glenmark Generics/ Telmisartan Glenmark 20, 40 and 80mg Film-coated Tablets
Type of Application	Generic, Article 10.1
Active Substance	Telmisartan
Form	Film-coated Tablets
Strength	20, 40 and 80mg
MA Holder	Glenmark Generics (Europe) Limited Laxmi House, 2 B Draycott Avenue, Kenton, Middlesex HA3 0BU, United Kingdom
RMS	UK
CMS	**UK/H/2633/001-3/DC** – Germany, Greece, Spain, France, Italy and The Netherlands **UK/H/4197/001-3/DC** – Germany and Italy **UK/H/4198/001-3/DC** – Austria, Belgium, Bulgaria, Germany, Denmark, Spain, Finland, France, Ireland, Italy, Luxemburg, The Netherlands, Portugal and Sweden
Procedure Numbers	UK/H/2633/001-3/DC UK/H/4197-8/001-3/DC
Timetable	Day 210 – 23rd March 2011

Module 2
Summary of Product Characteristics

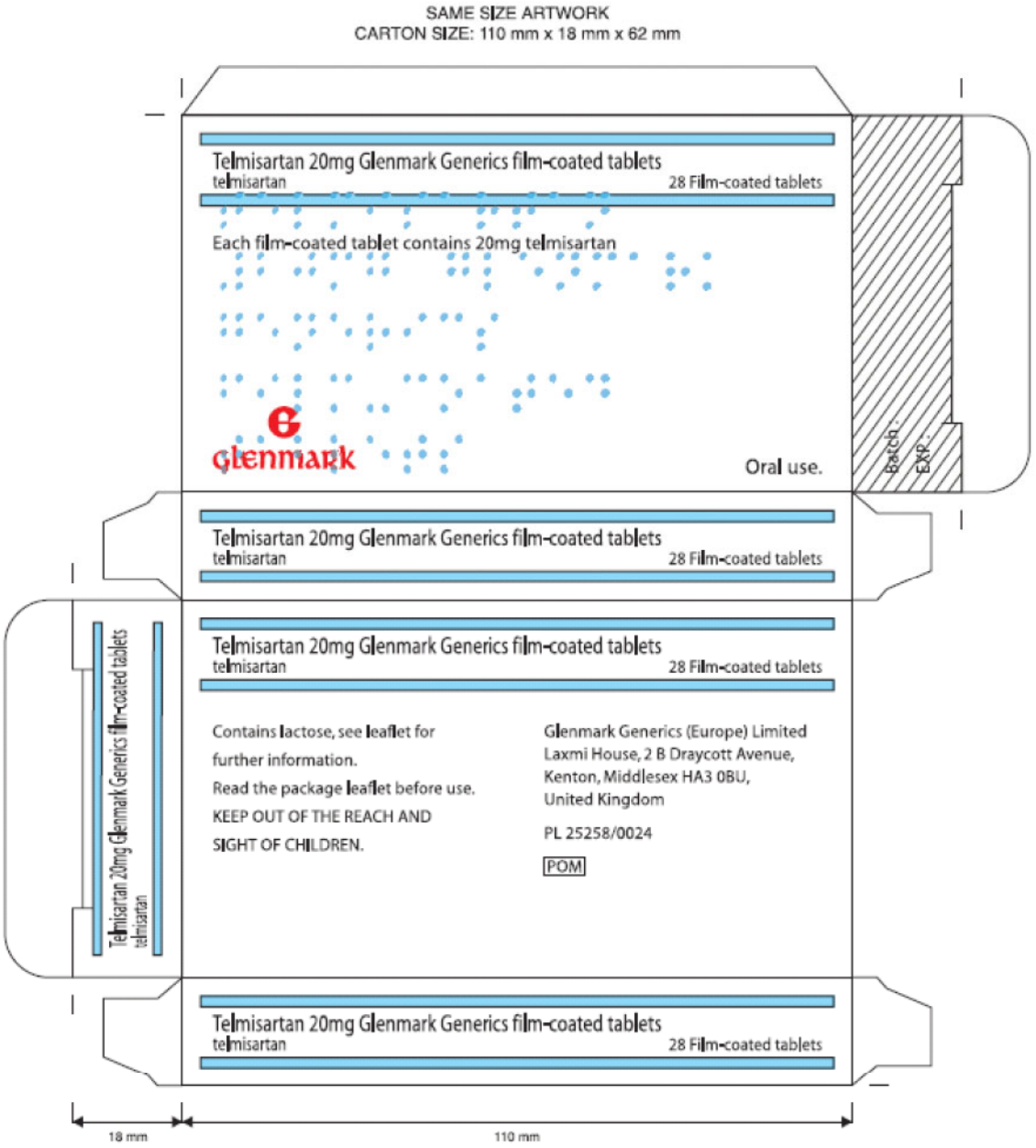
In accordance with Directive 2010/84/EU the Summary of Product Characteristics (SmPC) for products that have been granted Marketing Authorisations at a national level are available on the MHRA website.

Module 3
Patient Information Leaflet

In accordance with Directive 2010/84/EU the Patient Information Leaflets for products that are granted Marketing Authorisations at a national level are available on the MHRA website.

Module 4
Labelling

Below are representation mock-ups for PL 25258/0024-6




Telmisartan 20mg Glenmark Generics film-coated tablets
telmisartan
Glenmark Generics (Europe) Ltd
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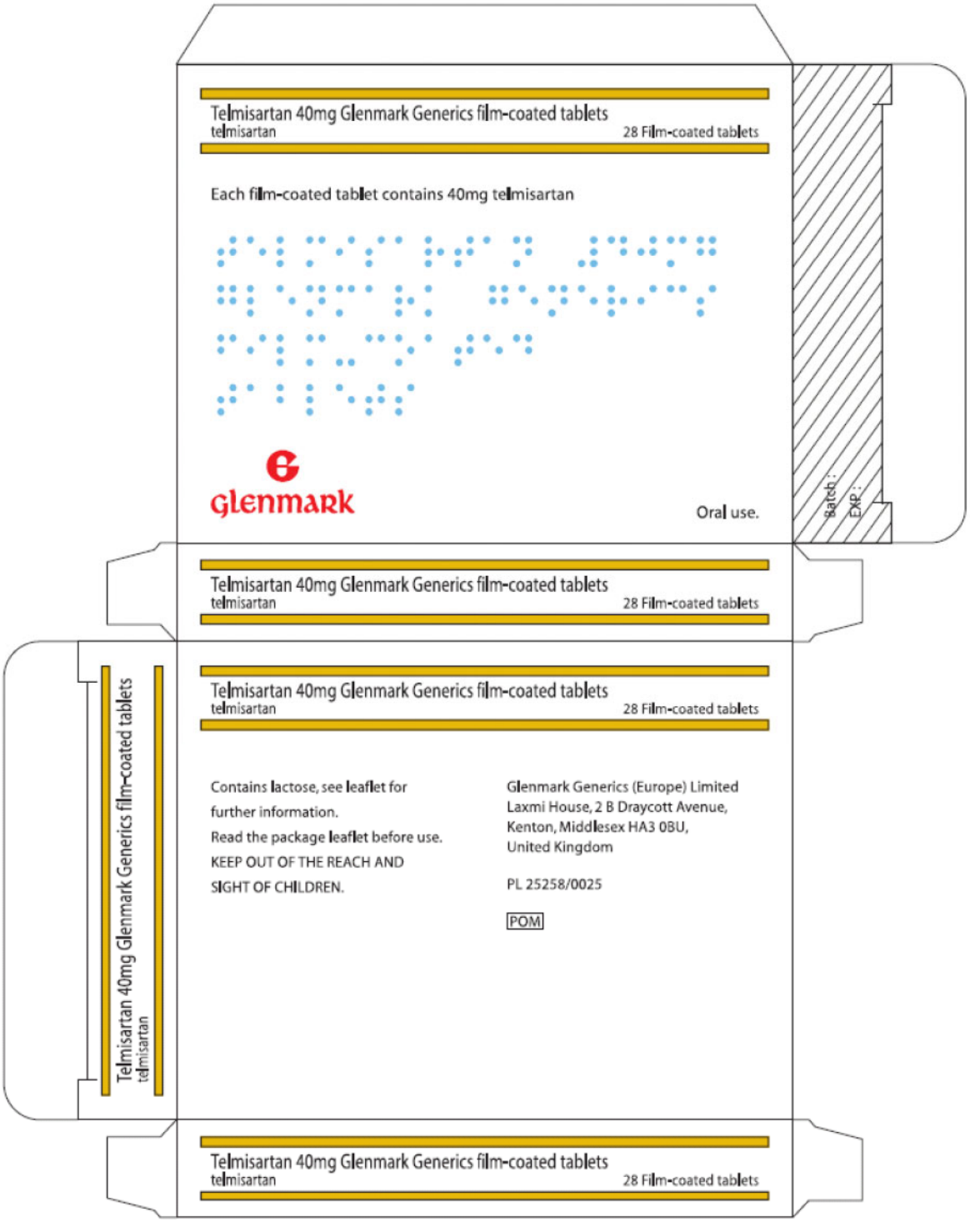
telmisartan
Glenmark Generics (Europe) Ltd
Telmisartan 20mg Glenmark Generics film-coated tablets
telmisartan
Glenmark Generics (Europe) Ltd


Telmisartan 40mg Glenmark Generics film-coated tablets
telmisartan
28 Film-coated tablets
Each film-coated tablet contains 40mg telmisartan
Glenmark
Oral use.
Batch :
EXP :
Telmisartan 40mg Glenmark Generics film-coated tablets
telmisartan
28 Film-coated tablets
Telmisartan 40mg Glenmark Generics film-coated tablets
telmisartan
28 Film-coated tablets
Contains lactose, see leaflet for further information.
Read the package leaflet before use.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Glenmark Generics (Europe) Limited
Laxmi House, 2 B Draycott Avenue,
Kenton, Middlesex HA3 0BU,
United Kingdom
PL 25258/0025
POM
Telmisartan 40mg Glenmark Generics film-coated tablets
telmisartan
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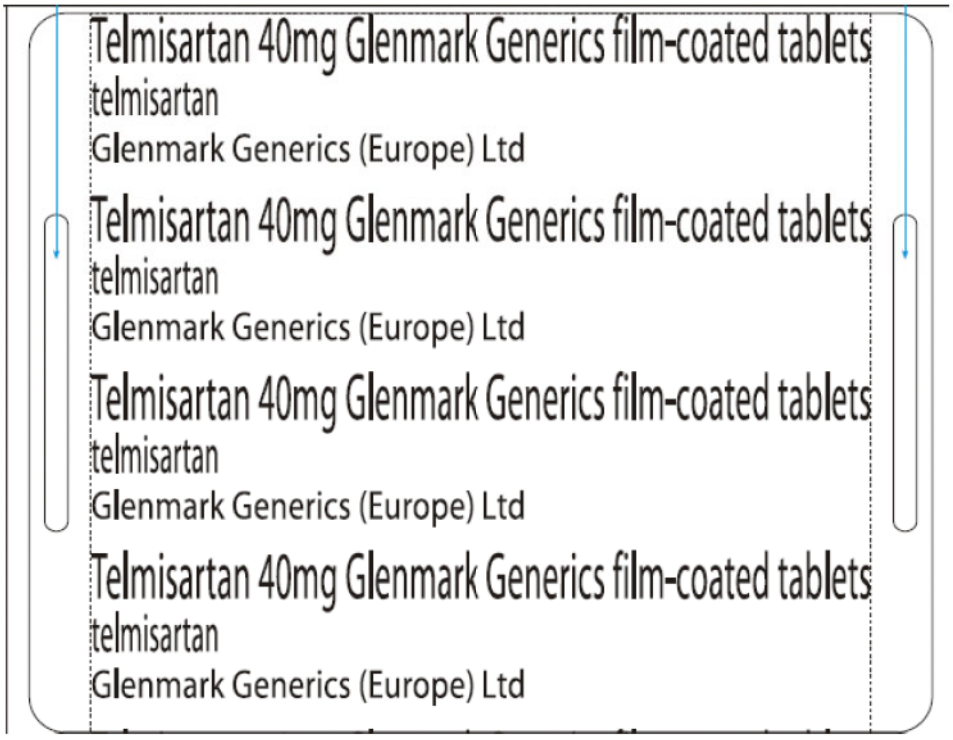
telmisartan
28 Film-coated tablets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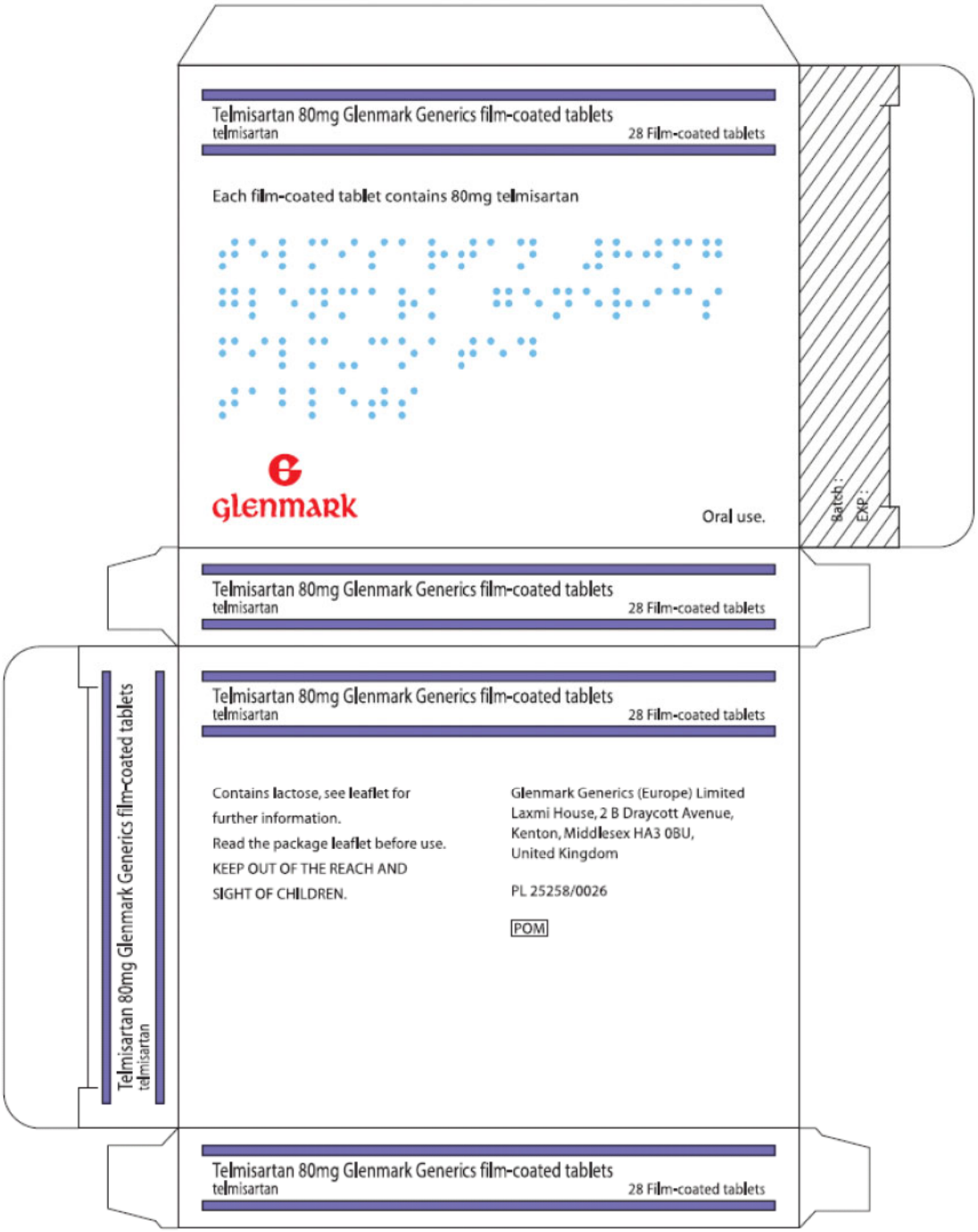
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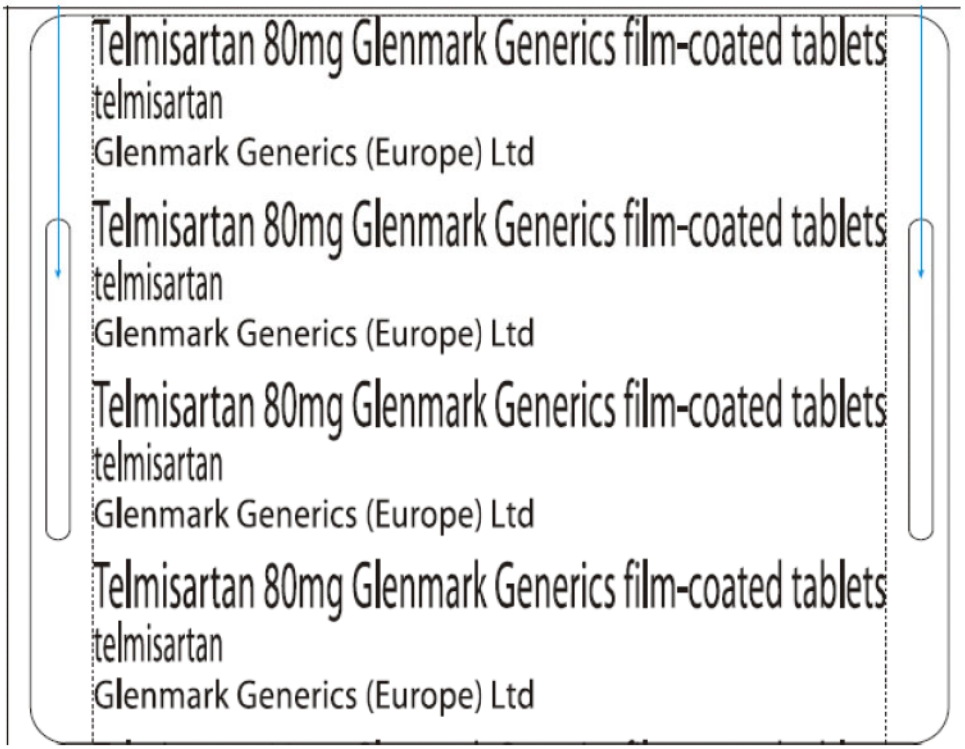
telmisartan
28 Film-coated tablets


Telmisartan 80mg Glenmark Generics film-coated tablets
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Glenmark Generics (Europe) Ltd
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telmisartan
Glenmark Generics (Europe) Ltd
Telmisartan 80mg Glenmark Generics film-coated tablets
telmisartan
Glenmark Generics (Europe) Ltd

Below are the text labels for PL 25258/0072-77

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Carton

1. NAME OF THE MEDICINAL PRODUCT

[Name to be completed nationally] 20mg film-coated tablets
[Name to be completed nationally] 40mg film-coated tablets
[Name to be completed nationally] 80mg film-coated tablets

telmisartan

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 20mg telmisartan
Each film-coated tablet contains 40mg telmisartan
Each film-coated tablet contains 80mg telmisartan

3. LIST OF EXCIPIENTS

Contains lactose, see leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablets
14 tablets
15 tablets
28 tablets
30 tablets
56 tablets
60 tablets
90 tablets
98 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:mm/yyyy

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally

12. MARKETING AUTHORISATION NUMBER(S)

13. BATCH NUMBER

Batch: XXXX

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Braille Text In Line with Directive 2001/83/EC (amended by Directive 2004/27/EC) Human use, Point 42, article 56a:

[Name to be completed nationally] 20mg film-coated tablets
[Name to be completed nationally] 40mg film-coated tablets
[Name to be completed nationally] 80mg film-coated tablets

The braille conversion is:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

[Name to be completed nationally] 20mg film-coated tablets
[Name to be completed nationally] 40mg film-coated tablets
[Name to be completed nationally] 80mg film-coated tablets
telmisartan

2. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally

3. EXPIRY DATE

EXP: mm/yyyy

4. BATCH NUMBER

Batch: xxxx

5. OTHER

Module 5
Scientific discussion during initial procedure

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Concerned Member States (CMSs) and Reference Member State (RMS) consider that the applications for Telmisartan Glenmark Generics/ Telmisartan Glenmark 20, 40 and 80mg Film-coated Tablets, in the treatment of essential hypertension in adults and reduction of cardiovascular morbidity in patients 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, could be approved.

These applications have been submitted under article 10(1) of Directive 2001/83/EC, as amended, as generic medicinal products, claiming essential similarity to Micardis 20, 40 and 80 mg film-coated tablets, which were first granted to Boehringer Ingelheim Limited, through centralised procedures, EU/1/98/090/009-012, in 1998.

With the UK as the Reference Member State in these Decentralized Procedures, Glenmark Generics (Europe) Limited applied for the Marketing Authorisations for Telmisartan Glenmark Generics/ Telmisartan Glenmark 20, 40 and 80mg Film-coated Tablets in the following CMSs:

UK/H/2633/001-3/DC – Germany, Greece, Spain, France, Italy and The Netherlands
UK/H/4197/001-3/DC – Germany and Italy
UK/H/4198/001-3/DC – Austria, Belgium, Bulgaria, Germany, Denmark, Spain, Finland, France, Ireland, Italy, Luxemburg, The Netherlands, Portugal and Sweden

Telmisartan is an orally active and specific angiotensin II receptor (type AT1) antagonist. Telmisartan displaces angiotensin II with very high affinity from its binding site at theAT1 receptor subtype, which is responsible for the known actions of angiotensin II.

No new preclinical and clinical studies were conducted, which is acceptable given that the applications were based on being generic medicinal products of originator products that have been licensed for over 10 years. Bioequivalence studies were carried out in accordance with Good Clinical Practice (GCP).

The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these product types at all sites responsible for the manufacture and assembly of this product.

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. A suitable justification has been provided for non-submission of a Risk Management Plan.

All Member States agreed to grant respective licence for the above products at the end of procedure (Day 210 – 23rd March 2011). After a subsequent national phase, the UK granted a licence for these products on 19th April 2011 (PL 25258/0024-6, 0072-77).

II. ABOUT THE PRODUCT

Name of the product in the Reference Member State	Telmisartan Glenmark Generics/ Telmisartan Glenmark 20, 40 and 80mg Film-coated Tablets
Name(s) of the active substance(s) (INN)	Telmisartan
Pharmacotherapeutic classification (ATC code)	C09CA07, Angiotensin II Antagonists, plain,
Pharmaceutical form and strength(s)	Film-coated Tablets, 20, 40 and 80mg
Reference numbers for the Decentralised Procedures	UK/H/2633/01-03/DC UK/H/4197-8/01-03/DC
Reference Member State	United Kingdom
Concerned Member States	**UK/H/2633/001-3/DC** – Germany, Greece, Spain, France, Italy and The Netherlands **UK/H/4197/001-3/DC** – Germany and Italy **UK/H/4198/001-3/DC** – Austria, Belgium, Bulgaria, Germany, Denmark, Spain, Finland, France, Ireland, Italy, Luxemburg, The Netherlands, Portugal and Sweden
Marketing Authorisation Number(s)	PL 25258/0024-6, 0072-77
Name and address of the authorisation holder	Glenmark Generics (Europe) Limited Laxmi House, 2 B Draycott Avenue, Kenton, Middlesex HA3 0BU, United Kingdom

III SCIENTIFIC OVERVIEW AND DISCUSSION

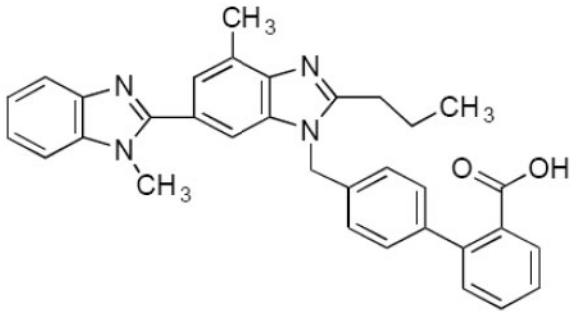
III.1 QUALITY ASPECTS

DRUG SUBSTANCE

INN: Telmisartan

Chemical Name: 4'-[[4 – methyl – 6 – (1 – methyl – 1*H* –benzimidazol – 2 – yl) – 2 – propyl – 1*H* – benzimidazol – 1 – yl] methyl]biphenyl – 2 – carboxylic acid

Structure:



Molecular Formula: $C_{33}H_{30}N_4O_2$

Molecular Weight: 514.6

Appearance: White or slightly yellowish, crystalline powder. Practically insoluble in water, slightly soluble in methanol, sparingly soluble in methylene chloride. It dissolves in 1M sodium hydroxide.

Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents, and these are supported by relevant certificates of analysis. Appropriate proof-of-structure data have been supplied. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the drug substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Certificates of Analysis for all working standards have been provided.

Batch analysis data are provided and comply with the proposed specification.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging used to store the drug substance. Confirmation has been provided that the primary packaging complies with current guidelines concerning materials in contact with food.

Appropriate stability data have been generated, supporting a suitable retest period when the drug substance is stored in the packaging proposed.

DRUG PRODUCT

Other Ingredients

Other ingredients consist of the pharmaceutical excipients sodium hydroxide, povidone (K-25), meglumine, lactose monohydrate, crospovidone, ferric oxide yellow (E172), magnesium stearate making up the tablet core; and (Opadry 02B82506 Yellow) hypromellose, titanium

dioxide (E171), macrogol-400, talc and ferric oxide yellow (E172) comprising the film-coating.

All excipients comply with their respective European Pharmacopoeia monographs except Opadry 02B82506 Yellow, which comply with an in-house specification and ferric oxide yellow (E172) which complies with United States Pharmacopoeia. Satisfactory Certificates of Analysis have been provided for all excipients.

It had been confirmed that the excipients used are free of TSE/BSE and the corresponding certificates issued by each supplier were suitably provided. This is acceptable.

Pharmaceutical Development
The objective of the development programme was to formulate robust, stable tablets that contain the same active ingredient as Micardis 20, 40 and 80mg tablets registered in the EU since 16/12/1988 via centralized procedure.

Comparative impurity and dissolution profiles have been presented for test and reference products.

Manufacture
A satisfactory batch formula has been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results. Process validation data on pilot-scale batches have been provided. The results are satisfactory. The applicant has committed to perform process validation on future production full-scale batches.

Finished Product Specification
The finished product specification is satisfactory. Test methods have been described and adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of Analysis have been provided for any working standards used.

Container-Closure System
The finished product is packed in Aluminium/aluminium blisters – Cold formable aluminium foil and hard tempered aluminium foil.
Pack sizes of 14, 15, 28, 30, 56, 60, 84, 90 or 98 tablets (PL 25258/0024-6)
Pack sizes of 14, 15, 28, 30, 56, 60, 90 or 98 tablets (PL 25258/0072-77)

Specifications and Certificates of Analysis for all packaging materials have been provided. These are satisfactory. All primary packaging complies with EU legislation regarding contact with food.

Stability
Finished product stability studies have been conducted in accordance with current guidelines and in the packaging proposed for marketing.

Based on the results, a shelf-life of 3 years with no special storage conditions has been set for these products. This is satisfactory.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labelling
The SmPC, PIL and labels are pharmaceutically acceptable.

User testing of the package leaflet has been accepted, based on a bridging report provided by the applicant making reference to the user-testing of the PIL for Perindopril Tablets as the parent PIL. 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.

The proposed artwork complies with the relevant 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.

The Marketing Authorisation Holder has stated that not all licensed pack sizes may be marketed. They have committed to submitting mock-ups for unmarketed pack sizes to the relevant regulatory authorities for approval before those packs are commercially marketed.

Marketing Authorisation Application (MAA) Forms
The MAA forms are pharmaceutically satisfactory.

Expert report
The pharmaceutical expert report has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

Conclusion
There are no objections to the approval of these products from a pharmaceutical point of view.

III.2 PRE-CLINICAL ASPECTS
The pharmacological, pharmacokinetic and toxicological properties of telmisartan are well-known.

No new preclinical data have been supplied with these applications and none are required for applications of this type. The pre-clinical expert report has been written by an appropriately qualified person and is a suitable summary of the pre-clinical aspects of the dossier.

A suitable justification has been provided for non-submission of environmental risk assessment.

There are no objections to the approval of these products from a preclinical point of view.

III.3 CLINICAL ASPECTS
Clinical Pharmacology
Pharmacokinetics
In support of this application, the marketing authorisation holder has submitted two bioequivalence studies with Telmisartan 20 mg (**Study GRF-BS-010-08**) and Telmisartan 80mg (**Study GRF-BS-011-08**) under fasting conditions comparing the test product with the reference product.

Study GRF-BS-010-08 (Telmisartan 20 mg)
An open label, single dose, randomized, two-period, two-treatment, two-sequence, crossover study performed to demonstrate the bioequivalence of Telmisartan 20mg tablets (test) and Micardis 20mg tablets (reference) in healthy male volunteers under fasting conditions.

A single dose of the investigational products (1 tablet of 20 mg or 80mg) was administered orally to each subject in each period with 240 ± 2 ml of water after an overnight fast. A washout period of 12 days was maintained between the two dosing days in each group.

Serial blood sampling before dosing and at 0.25, 0.50, 0.67, 0.83, 1.00, 1.33, 1.67, 2.00, 2.33, 2.67, 3.00, 3.33, 3.67, 4.00, 4.33, 4.67, 5.00, 5.50, 6.00, 8.00, 10.00, 12.00, 18.00, 24.00, 48.00 and 72.00 hours after drug administration was carried out in each group.

Results
Study GRF-BS-010-08 (Telmisartan 20 mg)

Table 1 Pharmacokinetic summary data of Telmisartan (N=41)

Parameters	Least Squares Means		Ratio	%CV	90% Confidence Interval	
	Test	Reference			Lower	Upper
C_{max} (ng/ml)	28	29.95	93.49	19.28	87.07	100.38
AUC $_{(0-t)}$ (ng.hr/mL)	398.61	402.95	98.92	13.40	94.13	103.96
AUC $_{(0-\infty)}$ (ng.hr/mL)	438.72	445.54	98.47	13.92	93.52	103.68

Study GRF-BS-011-08(Telmisartan 80 mg)
An open label, single dose, randomized, two-period, two-treatment, two-sequence, crossover study performed to demonstrate the bioequivalence of Telmisartan 80mg tablets (test) and Micardis 80mg tablets (reference) in healthy male volunteers under fasting conditions.

A single dose of the investigational products (1 tablet of 20 mg or 80mg) was administered orally to each subject in each period with 240 ± 2 ml of water after an overnight fast. A washout period of 12 days was maintained between the two dosing days in each group.

Serial blood sampling before dosing and at 0.25, 0.50, 0.67, 0.83, 1.00, 1.33, 1.67, 2.00, 2.33, 2.67, 3.00, 3.33, 3.67, 4.00, 4.33, 4.67, 5.00, 5.50, 6.00, 8.00, 10.00, 12.00, 18.00, 24.00, 48.00 and 72.00 hours after drug administration was carried out in each group.

Results
Study GRF-BS-011-08 (Telmisartan 80 mg)

Table 2 Pharmacokinetic summary data of Telmisartan (N=85)

Parameters	Least Squares Means		Ratio	%CV	90% Confidence Interval	
	Test	Reference			Lower	Upper
C_{max} (ng/ml)	338.95	370.09	91.58	41.46	82.73	101.38
AUC $_{(0-t)}$ (ng.hr/mL)	1666.31	1685.13	98.88	19.87	94.04	103.98
AUC $_{(0-\infty)}$ (ng.hr/mL)	1841.80	1874.85	98.24	18.81	93.67	103.03

The 90% confidence intervals for C_{max} and AUC were within the pre-defined limits (80-125%). Bioequivalence has been shown for the test formulations (Telmisartan 20mg and 80 mg Tablets) and the reference formulation (Micardis 20 mg and 80 mg Tablets). According to the Committee for Proprietary Medicinal Products Notes for Guidance on "Guideline on the Investigation of Bioequivalence" (CPMP/EWP/QWP/1401/98 Rev.1 Corr**), the results of the study for 20mg and 80mg formulation can be extrapolated to the other strength i.e 40mg Film-coated Tablets.

Pharmacodynamics
No new data have been submitted and none are required for these generic applications.

Clinical Efficacy
No new data have been submitted and none are required.

Clinical Safety
No new data have been submitted and none are required.

Expert Report
A clinical overall summary, written by an appropriately qualified physician, has been provided. This is a satisfactory, non-critical summary of Module 5.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling
The SmPC, PIL and labelling are medically satisfactory and consistent with those for the reference products.

Clinical Expert Report
The clinical expert report is written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

Marketing Authorisation Application (MAA) Forms
The MAA forms are medically satisfactory.

Clinical Conclusion
There are no objections to the approval of these products from a clinical point of view.

IV. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY

The important quality characteristics of Telmisartan Glenmark Generics/ Telmisartan Glenmark 20, 40 and 80mg Film-coated Tablets 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.

PRECLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

Bioequivalence have been demonstrated between the applicant's Telmisartan 20mg and 80 mg Tablets and the reference product, Micardis 20 mg and 80 mg Tablets and the results can be extrapolated to the 40mg Film-coated Tablets.

No new or unexpected safety concerns arise from these applications.

The SmPC and PIL are satisfactory and consistent with those of the reference products. Satisfactory labelling has also been submitted.

RISK-BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with telmisartan is considered to have demonstrated the therapeutic value of the compound. The risk-benefit is, therefore, considered to be positive.

Module 6

STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY

Date submitted	Application type	Scope	Outcome