Public Assessment Report

Decentralised Procedure

Telmisartan/Hydrochlorothiazide Dr. Reddy’s 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg Tablets

Telmisartan and Hydrochlorothiazide

UK/H/5035/001-3/DC

UK licence no: PL 08553/0481-83

Dr. Reddy’s Laboratories (UK) Ltd
LAY SUMMARY

On 10th May 2013, the Medicines and Healthcare products Regulatory Agency (MHRA) granted Marketing Authorisations (licences) to Dr. Reddy’s Laboratories (UK) Ltd for the medicinal products Telmisartan/Hydrochlorothiazide Dr. Reddy’s 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg Tablets (PL 08553/0481-83, UK/H/5035/001-3/DC). These are prescription-only medicines (POM).

Telmisartan/Hydrochlorothiazide is a combination of two active substances, telmisartan and hydrochlorothiazide in one tablet. Both of these substances help to control high blood pressure.

• Telmisartan belongs to a group of medicines called angiotensin II receptor antagonists. Angiotensin-II is a substance produced in your body which causes your blood vessels to narrow thus increasing your blood pressure. Telmisartan blocks the effect of angiotensin II so that the blood vessels relax and your blood pressure is lowered.

• Hydrochlorothiazide belongs to a group of medicines called thiazide diuretics, which cause your urine output to increase, leading to a lowering of your blood pressure.

High blood pressure, if not treated, can damage blood vessels in several organs, which could lead sometimes to heart attack, heart or kidney failure, stroke or blindness. There are usually no symptoms of high blood pressure before damage occurs. Thus it is important to regularly measure blood pressure to verify if it is within the normal range.

Telmisartan/Hydrochlorothiazide is used to treat high blood pressure (essential hypertension) in adults whose blood pressure is not controlled enough when either telmisartan or hydrochlorothiazide is used alone.

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Telmisartan/Hydrochlorothiazide Dr. Reddy’s 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg Tablets outweigh the risks. Hence Marketing Authorisations have been granted.
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### Module 1
**Information about initial procedure**

<table>
<thead>
<tr>
<th><strong>Product Name</strong></th>
<th>Telmisartan/Hydrochlorothiazide Dr. Reddy’s 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of Application</strong></td>
<td>Generic, Article 10.1</td>
</tr>
<tr>
<td><strong>Active Substance</strong></td>
<td>Telmisartan and hydrochlorothiazide</td>
</tr>
<tr>
<td><strong>Form</strong></td>
<td>Tablets</td>
</tr>
<tr>
<td><strong>Strength</strong></td>
<td>40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg Tablets</td>
</tr>
</tbody>
</table>
| **MA Holder** | Dr. Reddy’s Laboratories (UK) Ltd.  
6 Riverview Road  
Beverley  
East Yorkshire  
HU17 0LD  
United Kingdom |
| **RMS** | UK |
| **CMS** | Germany and Romania |
| **Procedure Numbers** | UK/H/5035/001-3/DC |
| **Timetable** | Day 210 – 21st April 2013 |
Module 2

SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) for products that are 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 (PILs) for products that are granted Marketing Authorisations at a national level are available on the MHRA website.
Module 4

Labelling

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

1. NAME OF THE MEDICINAL PRODUCT
   Telmisartan/Hydrochlorothiazide 40 mg/12.5 mg Tablets
   Telmisartan/Hydrochlorothiazide 80 mg/12.5 mg Tablets
   Telmisartan/Hydrochlorothiazide 80 mg/25 mg Tablets

2. NAME OF THE MARKETING AUTHORISATION HOLDER
   Dr. Reddy's Laboratories (UK) Ltd.

3. EXPIRY DATE
   EXP

4. BATCH NUMBER
   BN

5. OTHER
   n/a
PARTICULARS TO APPEAR ON THE OUTER PACKAGING CARTON LABEL.

1. NAME OF THE MEDICINAL PRODUCT
Telmisartan/Hydrochlorothiazide 40 mg/12.5 mg Tablets
Telmisartan/Hydrochlorothiazide 80 mg/12.5 mg Tablets
Telmisartan/Hydrochlorothiazide 80 mg/25 mg Tablets

2. STATEMENT OF ACTIVE SUBSTANCE(S)
Each tablet contains 40 mg telmisartan and 12.5 mg hydrochlorothiazide.
Each tablet contains 80 mg telmisartan and 12.5 mg hydrochlorothiazide.
Each tablet contains 80 mg telmisartan and 25 mg hydrochlorothiazide.

3. LIST OF EXCIPIENTS
Also contains lactose.

4. PHARMACEUTICAL FORM AND CONTENTS
28 tablets
56 tablets
98 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION
For 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 sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY
n/a

8. EXPIRY DATE
EXP

9. SPECIAL STORAGE CONDITIONS
This medicinal product does not require any special storage conditions.

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER
Dr. Reddy’s Laboratories (UK) Ltd., 6 Riverview Road, Beverley, HU17 0LD

12. MARKETING AUTHORISATION NUMBER(S)
PL 08553/0481
PL 08553/0482
PL 08553/0483

13. BATCH NUMBER
BN

14. GENERAL CLASSIFICATION FOR SUPPLY
POM
15. INSTRUCTIONS ON USE
Take as directed by your doctor.

16. INFORMATION IN BRAILLE
Telmisartan/Hydrochlorothiazide 40 mg/12.5 mg Tablets
Telmisartan/Hydrochlorothiazide 80 mg/12.5 mg Tablets
Telmisartan/Hydrochlorothiazide 80 mg/25 mg Tablets
Module 5
Scientific discussion during initial procedure

I  INTRODUCTION
Based on the review of the data on quality, safety and efficacy, the Reference Member State (RMS) and Concerned Member States (CMSs) consider that the applications for Telmisartan/Hydrochlorothiazide Dr. Reddy’s 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg Tablets in the treatment of essential hypertension, could be approved.

These applications were submitted under Article 10.1 of Directive 2001/83/EC, as amended for Telmisartan/Hydrochlorothiazide Dr. Reddy’s 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg Tablets, claiming to be generic medicinal products of Micardis Plus® 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg Tablets (EU/1/02/213/001-023), which were first licensed to Boehringer Ingelheim International GmbH, on 19th April 2002 via a centralised procedure.

With UK as the RMS in these Decentralised Procedures (UK/H/5035/001-3/DC), Dr. Reddy’s Laboratories (UK) Ltd applied for the Marketing Authorisations for Telmisartan/Hydrochlorothiazide Dr. Reddy’s 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg Tablets in Germany and Romania.

Telmisartan is a long-acting, non-peptide angiotensin II receptor-subtype 1 (AT₁) antagonist, which is orally active, highly selective, and potent. The blood pressure lowering effect is mediated via specific blockade of the A-II Type 1 (AT₁) receptor, which reduces the arterial pressure response to A-II, restricts sodium reabsorption and has multiple actions at other sites.

Hydrochlorothiazide is thiazide diuretic and a sulphonamide derivative. Hydrochlorothiazide has been in clinical use in UK, Europe and indeed worldwide for a number of years as an antihypertensive, both as a single agent and of late, in combination with many other antihypertensives of different classes including, ACE inhibitors, ARBS such as Telmisartan, beta-blockers and some calcium channel blockers. The mechanism of the antihypertensive effect of thiazides is not fully elucidated although these agents act by promoting sodium excretion leading to a transitory negative sodium balance. Thiazides affect the renal tubular mechanisms of electrolytes reabsorption in the distal segment of the nephron, directly increasing the excretion of sodium and chloride in approximately equivalent amounts by blocking the Na⁺Cl⁻ co-transporter.

No new non-clinical or 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. The 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 these products.

For manufacturing sites inside and outside the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities
as certification that acceptable standards of GMP are in place at those sites.

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 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 licences for the above products at the end of the procedure (Day 210 – 21st April 2013). After a subsequent national phase, the UK granted licences for these products on 10th May 2013 (PL 08553/0481-83).
### II. ABOUT THE PRODUCT

| Name of the product in the Reference Member State | Telmisartan/Hydrochlorothiazide Dr. Reddy’s 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg Tablets |
| Name(s) of the active substance(s) (INN) | Telmisartan and hydrochlorothiazide |
| Pharmacotherapeutic classification (ATC code) | Group: Angiotensin II receptor antagonists and diuretics, ATC code: C09DA07 |
| Pharmaceutical form and strength(s) | Tablet, 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg |
| Reference numbers for the Decentralised Procedures | UK/H/5035/001-3/DC |
| Reference Member State | United Kingdom |
| Concerned Member States | Germany and Romania |
| Marketing Authorisation Number(s) | PL 08553/0481-83 |
| Name and address of the authorisation holder | Dr. Reddy’s Laboratories (UK) Ltd. 6 Riverview Road Beverley East Yorkshire HU17 0LD United Kingdom |
III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 QUALITY ASPECTS

DRUG SUBSTANCE

INN: Telmisartan

Chemical Names:
[1,1’ -Biphenyl]-2-carboxylic acid, 4’ - [(1,4’ -dimethyl-2’ –propyl [2,6’ -bi-1H-
benzimidazol]-1’ -yl)methyl;
[or]
4’ -[(1,4’ -Dimethyl-2’ -propyl[2,6’ -bi-IH-benzimidazol]-I’ -yl)methyl]-[I, I’ -biphenyl]-2-
carboxylic acid.
[or]
4’ -[[4-methyl-6-(I-methyl-2-benzimidazolyl)-2-propyl-Ibenzimidazolyl] methyl]-2-biphenyl
carboxylic acid.
[or]
4’ -[[4-Methyl-6-(1-Methyl-IH-benzimidazol-2-yl)-2propyl-IHbenzimidazol-I-
yl]methyl]biphenyl-2-carboxylic acid (Ph Eur name)

Structure:

![Structure of Telmisartan]

Molecular Formula: C$_{33}$H$_{30}$N$_{4}$O$_{2}$
Molecular Weight: 514.62

Appearance: White to slightly yellowish coloured powder.
Solubility: Sparingly soluble in methylene chloride.

Telmisartan is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance telmisartan are covered by
a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of
Suitability.

INN: Hydrochlorothiazide

Chemical Names: 6-Chloro-3,4-dihydro-2$H$-1,2,4-benzothiadiazine-7-sulfonamide 1,1-
dioxide
Structure:

\[
\begin{array}{c}
\text{O} \\
\text{N} \\
\text{S} \\
\text{O} \\
\text{H}_2 \text{N} \\
\text{Cl} \\
\text{N} \\
\end{array}
\]

Molecular Formula: C$_7$H$_5$C1N$_3$O$_4$S$_2$
Molecular Weight: 297.74

Appearance: A white or almost white, crystalline powder.
Solubility: slightly soluble in water, freely soluble in sodium hydroxide solution

Hydrochlorothiazide is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance hydrochlorothiazide are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

**DRUG PRODUCT**

**Other Ingredients**

Other ingredients consist of the pharmaceutical excipients meglumine, sodium hydroxide, povidone (K-30), polysorbate 80, mannitol, magnesium stearate, lactose monohydrate and Iron oxide red (E172).

All excipients comply with their respective European Pharmacopoeia monographs with the exception of Iron oxide red (E172) which is covered by a National formulary. Satisfactory Certificates of Analysis have been provided for all excipients.

The only excipient used that contains material of animal or human origin is lactose monohydrate. The applicant has provided a declaration that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption. Confirmation has also been given that the magnesium stearate used in the tablets is of vegetable origin.

**Pharmaceutical Development**

The objective of the development programme was to formulate robust, stable tablets that contain the same active ingredient as Micardis Plus® 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg Tablets, Boehringer Ingelheim International GmbH.

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

**Manufacture**

Satisfactory batch formulae have 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. Satisfactory process validation data on
pilot-scale batches have been provided. The applicant has committed to perform process validation on future commercial-scale batches.

**Finished Product Specification**
The finished product specification is satisfactory. Test methods have been described and adequately validated. 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 Alu/Alu blisters (OPA/Alu/PVC-Alu) with pack sizes of 28, 56 or 98 tablets.

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 2 years has been set. These medicinal products do not require any special storage conditions. This is satisfactory.

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

A package leaflet has been submitted to the MHRA together with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that the package leaflet contains.

**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 NON-CLINICAL ASPECTS**
The pharmacodynamic, pharmacokinetic and toxicological properties of telmisartan and hydrochlorothiazide are well known.

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

A suitable justification has been provided for non-submission of an environmental risk assessment. This is satisfactory.

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

### III.3 CLINICAL ASPECTS

#### Clinical Pharmacology

##### Pharmacokinetics

In support of these applications, the Marketing Authorisation Holder has submitted two bioequivalence studies with 80/12.5 mg and 80/25 mg strengths.

**Study 1 (H166-10)**  
This is an open label, balanced, randomized, two-treatment, two-sequence, two-period, single dose, crossover oral bioequivalence study of Telmisartan/hydrochlorothiazide 80 mg /25 mg tablets (Dr. Reddy’s Laboratories Limited, India) and Micardis plus® 80 mg/25 mg tablets (Boehringer Ingelheim, International GmbH & Co.KG, Deutschland), in normal, healthy, adult, human subjects under fasting conditions.

Twenty three samples were collected from each subject during each period. The venous blood samples (05 mL each) were withdrawn at pre-dose (before dosing, in the morning of the day of dosing) and at 0.17, 0.33, 0.50, 0.75, 1.00, 1.33, 1.67, 2.00, 2.33, 2.67, 3.00, 3.50, 4.00, 5.00, 6.00, 8.00, 12.00, 16.00, 24.00, 36.00, 48.00 and 72.00 hours after dosing. Sample scheduled at 72.00 hours after dosing were collected on ambulatory basis (i.e., on separate visits). There was a washout period of 12 days between study drug administrations.

#### Results

**Pharmacokinetic parameters (Log-transformed values; Geometric mean ± SD) for Telmisartan**

<table>
<thead>
<tr>
<th>PK Parameters</th>
<th>Geometric Least Square Means</th>
<th>Log Transformed PK Values</th>
<th>90% Confidence Interval</th>
<th>Power (%)</th>
<th>ISC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test (T)</td>
<td>Reference (R)</td>
<td>T/R Ratio (%)</td>
<td>LCL</td>
<td>UCL</td>
</tr>
<tr>
<td>C_{max} (ng/mL)</td>
<td>441.4153</td>
<td>414.3252</td>
<td>106.54</td>
<td>97.88</td>
<td>115.96</td>
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<tr>
<td>AUC_{0-t} (ng hr/mL)</td>
<td>2158.3200</td>
<td>2033.8458</td>
<td>106.12</td>
<td>102.11</td>
<td>110.29</td>
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<tr>
<td>AUC_{0-t,INF} (ng hr/mL)</td>
<td>2394.3426</td>
<td>2225.8189</td>
<td>107.57</td>
<td>103.41</td>
<td>111.90</td>
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Pharmacokinetic parameters (Log-transformed values; Geometric mean ± SD) for Hydrochlorothiazide

<table>
<thead>
<tr>
<th>PK Parameters</th>
<th>Log Transformed PK Values</th>
<th>90% Confidence Interval</th>
<th>Power (%)</th>
<th>ISC V (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Geometric Least Square Means</td>
<td>T/R Ratio (%)</td>
<td>LCL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test (T)</td>
<td>Reference (R)</td>
<td>UCL</td>
<td></td>
</tr>
<tr>
<td>C\text{max} (ng/mL)</td>
<td>162.1048</td>
<td>178.0961</td>
<td>91.02</td>
<td>86.50</td>
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<tr>
<td>AUC_{0-t} (ng hr/mL)</td>
<td>1251.7759</td>
<td>1375.0251</td>
<td>91.04</td>
<td>88.13</td>
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<tr>
<td>AUC_{0-\infty} (ng hr/mL)</td>
<td>1284.1851</td>
<td>1408.9789</td>
<td>91.14</td>
<td>88.27</td>
</tr>
</tbody>
</table>

The 90% confidence intervals for $C_{\text{max}}$ and AUC were within the pre-defined limits. Bioequivalence has been shown for the test formulation (Telmisartan/hydrochlorothiazide 80 mg /25 mg tablets) and the reference formulation (Micardis plus® 80 mg/25 mg tablets).

Study 2 (H233-11)
This is an open label, balanced, randomized, two-treatment, two-sequence, two-period, single-dose, crossover oral bioequivalence study of Telmisartan/Hydrochlorothiazide tablets 80 mg/12.5 mg (Dr. Reddy's Laboratories Limited, India) and Micardis plus® 80 mg/12.5 mg tablets (Boehringer Ingelheim Pharma GmbH & Co.KG, Deutschland), in normal, healthy, adult, human subjects under fasting condition.

Twenty three samples were collected from each subject during each period. The venous blood samples (05 mL each) were withdrawn at pre-dose (before dosing, in the morning of the day of dosing) and at 0.17, 0.33, 0.50, 0.75, 1.00, 1.33, 1.67, 2.00, 2.33, 2.67, 3.00, 3.50, 4.00, 5.00, 6.00, 8.00, 12.00, 16.00, 24.00, 36.00, 48.00 and 72.00 hours after dosing. Sample scheduled at 72.00 hours after dosing were collected on ambulatory basis (i.e., on a separate visit). There was a washout period of 12 days between study drug administrations.

Results
Pharmacokinetic parameters (Log-transformed values; Geometric mean ± SD) for Telmisartan

<table>
<thead>
<tr>
<th>PK Parameters</th>
<th>Log Transformed PK Values</th>
<th>90% Confidence Interval</th>
<th>Power (%)</th>
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<tbody>
<tr>
<td></td>
<td>Geometric Least Square Means</td>
<td>T/R Ratio (%)</td>
<td>LCL</td>
<td></td>
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<tr>
<td></td>
<td>Test (T)</td>
<td>Reference (R)</td>
<td>UCL</td>
<td></td>
</tr>
<tr>
<td>$C_{\text{max}}$ (ng/mL)</td>
<td>433.6532</td>
<td>415.1148</td>
<td>104.47</td>
<td>94.02</td>
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<tr>
<td>AUC_{0-t} (ng hr/mL)</td>
<td>2430.7150</td>
<td>2388.4223</td>
<td>101.77</td>
<td>97.51</td>
</tr>
</tbody>
</table>
Pharmacokinetic parameters (Log-transformed values; Geometric mean ± SD) for Hydrochlorothiazide

<table>
<thead>
<tr>
<th>PK Parameters</th>
<th>Log Transformed PK Values</th>
<th>90% Confidence Interval</th>
<th>Power (%)</th>
<th>ISC V (%)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Geometric Least Square Means</td>
<td>T/R Ratio (%)</td>
<td>LCL</td>
<td>UCL</td>
</tr>
<tr>
<td>C_{max} (mg/mL)</td>
<td>71.4263</td>
<td>93.20</td>
<td>89.01</td>
<td>97.59</td>
</tr>
<tr>
<td>AUC_{0-t} (ng h/mL)</td>
<td>525.3113</td>
<td>95.16</td>
<td>91.27</td>
<td>99.22</td>
</tr>
</tbody>
</table>

The 90% confidence intervals for C_{max} and AUC were within the pre-defined limits. Bioequivalence has been shown for the test formulation (Telmisartan/hydrochlorothiazide 80 mg/12.5 mg tablets) and the reference formulation (Micardis plus® 80 mg/12.5 mg tablets).

According to the Committee for Proprietary Medicinal Products Notes for Guideline on “Guideline on the Investigation of Bioequivalence” (CPMP/EWP/QWP/1401/98 Rev.1 Corr**), the results of the study for 80 mg/25 mg and 80 mg/12.5 mg formulations can be extrapolated to the other strength i.e. 40 mg/12.5 mg Tablets.

**Pharmacodynamics**
No new data have been submitted and none are required for applications of this type.

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

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

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

**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/Hydrochlorothiazide Dr. Reddy’s 40 mg/12.5 mg, 80 mg/12.5 mg and 80 mg/25 mg 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.

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

EFFICACY
Bioequivalence has been demonstrated between the applicant’s Telmisartan/hydrochlorothiazide 80 mg /25 mg tablets and Telmisartan/hydrochlorothiazide 80 mg /12.5 mg tablets and the reference products, Micardis plus® 80 mg/25 mg tablets and . Micardis plus® 80 mg/12.5 mg tablets. According to the Committee for Proprietary Medicinal Products Notes for Guideline on “Guideline on the Investigation of Bioequivalence” (CPMP/EWP/QWP/1401/98 Rev.1 Corr**), the results of the study for 80 mg/25 mg and 80 mg/12.5 mg formulations can be extrapolated to the other strength i.e. 40 mg/12.5 mg Tablets.

No new or unexpected safety concerns arose from these applications.

The SmPCs 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 non-clinical or clinical safety concerns have been identified. Extensive clinical experience with telmisartan and hydrochlorothiazide is considered to have demonstrated the therapeutic value of the product. The risk-benefit is, therefore, considered to be positive.
Module 6

STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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