LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Telmisartan Amarox
(telmisartan)

SE/H/2764/001-003/DC

This module reflects the scientific discussion for the approval of Telmisartan Amarox. The procedure was finalised at 2026-05-20. For information on changes after this date please refer to the module 'Steps taken after the finalisation of the initial procedure - Summary'.

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TABLE OF CONTENTS

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have agreed to grant a marketing authorisation for Telmisartan Amarox, 20 mg, 40 mg, 80 mg, Tablet.

The active substance is telmisartan. A comprehensive description of the indication and posology is given in the SmPC.

II. EXECUTIVE SUMMARY

II.1 About the product

Telmisartan is an angiotensin II receptor blocker and selectively binds the AT1 receptor. The binding is long-lasting and result in reductions of blood pressure. Telmisartan Amarox is indicated for treatment of essential hypertension in adults and cardiovascular prevention. The proposed posology is 40 mg daily (hypertension) respectively 80 mg daily (cardiovascular prevention).

II.2 General comments on the submitted dossier

The application for Telmisartan Amarox, 20 mg, 40 mg, 80 mg, Tablet, is a Generic Art. 10(1) application submitted according to Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and BG, CZ, DE, EE, EL, ES, FI, FR, HU, IE, IT, NL, PL, PT, RO, SI, SK as concerned member states (CMS). BE was initially a CMS, but the application was withdrawn there during clockstop.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Micardis, 20 mg, tablets, authorised in the Union since 1999, with Boehringer Ingelheim International GmbH as marketing authorisation holder.

The reference product used in the bioequivalence study is Micardis, 80 mg, tablets, from DE with Boehringer Ingelheim International GmbH as marketing authorisation holder.

II.3 General comments on compliance with GMP, GLP, GCP and agreed ethical principles

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product.
For manufacturing sites within 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.

For manufacturing sites outside the Community, the RMS has accepted copies of current GMP Certificates of satisfactory inspection summary reports, ‘close-out letters’ or ‘exchange of information’ issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community sites.

GMP active substance
Regarding the statement on GMP for the active substance a QP declaration is provided from the manufacturer(s) responsible for manufacture of the finished product and batch release situated in the EU.

GCP aspects
A statement on the application of appropriate GCP standards in the submitted study has been provided. No issues regarding GCP have been identified. The submitted inspection reports have been reviewed and based on these there are no further questions regarding GCP quality at the sites where the study was performed. No inspection of the submitted bioequivalence study is needed.

III. SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 Quality aspects

Drug substance
The structure of the drug substance has been adequately proven, and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described, and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

Drug Product
The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III.2 Non-clinical aspects

Pharmacology/Pharmacokinetics/Toxicology
Pharmacodynamic, pharmacokinetic and toxicological properties of telmisartan are well known. As telmisartan is a widely used, well-known active substance, no further studies are required, nor does the applicant provide any. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
The Applicant has submitted an environmental risk assessment (ERA). However, the provided ERA report is not in line with the current version of the guideline.

Phase I
The PECsw value is 0.4 µg/L. A Phase II risk assessment is required.

Phase II
A Phase II Tier A risk assessment could not be identified in report. Consequently, a definitive conclusion on the Phase II assessment cannot currently be drawn.

PBT
Telmisartan has been considered persistent, given that the half-life in sediment exceeds 120 days. The PBT assessment cannot be completed adequately, as the KOC*sludge* value (OECD 106) is missing. Submission of additional studies may be required.

No definitive conclusion on the environmental risks of telmisartan can be drawn at this moment. Therefore, Applicant has provided a separate commitment letter stating that an updated ERA will be provided within 5 years after the end of this procedure.

There are no objections to approval of Telmisartan Amarox from a non-clinical point of view.

III.3 Clinical aspects

Pharmacokinetics
To support the marketing authorisation application the applicant has conducted one bioequivalence study comparing Telmisartan Amarox (Telmisartan) with the reference product Micardis.

Pharmacokinetic properties of the active substance
Absorption:
Absorption of telmisartan is rapid although the amount absorbed varies. The mean absolute bioavailability for telmisartan is about 50%. When telmisartan is taken with food, the reduction in the area under the plasma concentration-time curve ($AUC_{0-\infty}$) of telmisartan varies from approximately 6% (40 mg dose) to approximately 19% (160 mg dose). By 3 hours after administration, plasma concentrations are similar whether telmisartan is taken fasting or with food. There are no restrictions with respect to food in the SmPC of the originator.

Telmisartan was rapidly absorbed after oral administration as solution, capsule or tablet. The time to peak plasma concentrations, t_{max}, was in the range of 0.5-3.0 hours and tended to decrease with higher doses.

Linearity/non-linearity:
There is no linear relationship between doses and plasma levels. C_{max} and to a lesser extent AUC increase disproportionately with dose at doses above 40 mg.

Elimination:
Telmisartan is characterised by biexponential decay pharmacokinetics with a terminal elimination half-life of > 20 hours.

Study C1B04776
Methods
This was a four-period, two-treatment, two-sequence, fully replicate, crossover, single-dose study conducted in 44 healthy volunteers, comparing Telmisartan, 80 mg, tablet with Micardis, 80 mg, tablet under fasting conditions. Blood samples for concentration analysis were collected pre-dose and up to 72 hours post-dose. Plasma concentrations of telmisartan were determined with a LC-MS/MS method. Analysis of variance (ANOVA) was performed on the ln-transformed data for AUC_{0-t} and C_{max}. The

study was conducted between 22-Oct-2024 and 08-Dec-2024.

Results
The results from the pharmacokinetic and statistical analysis are presented in Table 1 below.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} median, range) for telmisartan, n=79.

Treatment	AUC_{0-t} ng*h/ml	C_{max} ng/ml	t_{max} h
Test	**3952.089 (±2776.973)**	**644.650 (±568.716)**	**1.000 (0.500-4.333)**
Reference	**3814.202 (±2722.110)**	**658.177 (±513.798)**	**0.750 (0.500-4.333)**
***Ratio (90% CI)**	**97.78 (90.47-105.68)**	**90.37 (79.07-103.28)**	**-**

AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours
C_{max} maximum plasma concentration
t_{max} time for maximum plasma concentration

**calculated based on ln-transformed data*

For AUC_{0-t} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

For C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the widened acceptance range of 69.84-143.19%.

A biowaiver was sought for the additional strengths of 20 mg and 40 mg.

Discussion and overall conclusion
The bioequivalence study and its statistical evaluation were in accordance with accepted standards for bioequivalence testing, as stated in the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1) and ICH M13A Guideline on bioequivalence for immediate-release solid oral dosage forms (EMA/CHMP/ICH/953493/2022).

It was pre-specified in the protocol that widened acceptance criteria could be applied to C_{max}. The reference product within-subject variability was greater than 30% for C_{max} (51.151%). The calculated intra-subject variability was a reliable estimate, and not the result of outliers. A justification that the widened acceptance range for C_{max} is considered clinically irrelevant was provided. The bioanalytical method was adequately validated.

Based on the submitted bioequivalence study, Telmisartan Amarox is considered bioequivalent with Micardis.

Absence of studies with the additional strengths of 20 mg and 40 mg is acceptable, as all conditions for biowaiver for additional strength(s), as described in the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1) are fulfilled and as the plasma exposure of telmisartan increases more than proportional to dose in the therapeutic dose range.

Pharmacodynamics/Clinical efficacy/Clinical safety
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the originator product is demonstrated, additional data is not necessary.

Pharmacovigilance system
Proposed MAH: Amarox Pharma B.V. and affiliates
The Applicant has submitted a revised signed Summary of the Applicant's/Proposed Future MAH's Pharmacovigilance System in which all relevant subsidiaries are listed. Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation and as detailed in the GVP module, the RMS considers the Summary acceptable.

Risk Management Plan
The MAH has submitted an updated 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 Telmisartan Amarox.

Part II Safety specification
The MAH has submitted the version 0.3 RMP dated 23 Mar 2026 and proposed none safety concerns.

Part III Pharmacovigilance Plan
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Part V Risk minimisation measures
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Part VI Summary of the RMP
The Summary of the RMP is endorsed.

Conclusion RMP assessment
The submitted Risk Management Plan, version 0.2 RMP dated 21 Oct 2025 is considered acceptable if the safety concerns are removed.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

Periodic Safety Update Report (PSUR)
Active substance is currently listed in the published EURD list

With regard to PSUR submission, the MAH should take the following into account:

- PSURs shall be submitted 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. Marketing authorisation holders shall

continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.

- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.

- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

Common renewal date
The common renewal date will be 5 years after closure of the DCP.

IV. BENEFIT RISK ASSESSMENT

The quality of the generic product, Telmisartan Amarox, is found adequate. There are no objections to approval of Telmisartan Amarox, from a non-clinical and clinical point of view. Bioequivalence between the test and reference product has been adequately demonstrated. The product information is acceptable. The benefit/risk is considered positive, and the application is therefore recommended for approval.

V. RECOMMENDATIONS AND CONDITIONS FOR MARKETING AUTHORISATION AND PRODUCT INFORMATION

V.1 List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC

Post approval commitments
Applicant has committed to submit an updated Environmental Risk Assessment (ERA) for Telmisartan. The updated ERA will be provided within five (5) years following the completion of the current regulatory procedure, SE/H/2764/001-003/DC. The updated ERA will consider any relevant new scientific data, post-marketing information, and advancements in regulatory guidance available at the time of submission. The Applicant will remain committed to ensuring that the environmental risk profile of Telmisartan Tablets 20 mg, 40 mg, 80 mg is continuously evaluated in line with applicable regulatory requirements.

V.2 List of conditions pursuant to Article 21a or specific obligations pursuant to Article 22 of Directive 2001/83/EC

- **Additional risk minimisation measures (including educational material)**

  N/A

- **Obligation to conduct post-authorisation measures in accordance with Article 21a of Directive 2001/83/EC**

  N/A

- **Specific obligation to complete post-authorisation measures for the marketing authorisation under Exceptional circumstances in accordance with Article 22 of Directive 2001/83/EC**

  N/A

V.3 Summary of Product Characteristics (SmPC)

The approved SmPC is available in the MRI Product Index.

V.4 Package Leaflet (PL)

V.4.1 Package Leaflet

The approved PL is available in the MRI Product Index.

V.4.2 Assessment of User Testing

A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of a bridging report making reference to Micardis 20 mg, 40 mg & 80 mg tablets, EMEA/H/C/000209 and Levetiracetam Hetero 750 mg Film-Coated Tablets, PT/H/515/01-04/DC. The bridging report submitted by the applicant has been found acceptable.

VI. STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
-	-	-	-	-	-