COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Perindopril tosilaat/Indapamide DOC 2.5 mg/0.625 mg, 5 mg/1.25 mg and 10 mg/2.5 mg, film-coated tablets

(perindopril tosilate/indapamide)

NL/H/5718/001-003/DC

Date: 2 January 2026

This module reflects the scientific discussion for the approval of Perindopril tosilaat/Indapamide DOC 2.5 mg/0.625 mg, 5 mg/1.25 mg and 10 mg/2.5 mg, film-coated tablets. The procedure was finalised on 6 March 2024. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Perindopril tosilaat/Indapamide DOC 2.5 mg/0.625 mg, 5 mg/1.25 mg and 10 mg/2.5 mg, film-coated tablets, from DOC Generici S.r.l.

The product is indicated:

- 2.5 mg/0.625 mg strength
  in the treatment of essential hypertension in adults.
- 5 mg/1.25 mg strength
  in the treatment of essential hypertension in adults patients whose blood pressure is not adequately controlled on perindopril alone.
- 10 mg/2.5 mg strength
  as substitution therapy for treatment of essential hypertension, in patients already controlled with perindopril and indapamide given concurrently at the same dose level.

A comprehensive description of the up-to-date indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC, which concerns a generic application.

In this decentralised procedure, essential similarity is proven between the new product and the reference product Preterian 2.5 mg/0.625 mg, film-coated tablets. The reference product has been registered by Les Laboratoires Servier in France on 25 November 1997 as perindopril tert-butylamine/indapamide (FR/H/130/001), also named Preterax, BiPreterax N, Noliterax or Coversyl Plus in other member states. The reference product nowadays contains the more stable perindopril arginine as salt form, while the product at stake contains perindopril tosilate.

The concerned member state (CMS) involved in this procedure was Italy.

II. QUALITY ASPECTS

II.1 Introduction

Perindopril tosilaat/Indapamide DOC is a film-coated tablet. Each tablet contains as active substances:

- 2.5 mg/0.625 mg strength
  2.5 mg perindopril tosilate corresponding to 1.704 mg perindopril, converted in situ to perindopril sodium, and 0.625 mg indapamide.
- 5 mg/1.25 mg strength
  5 mg perindopril tosilate corresponding to 3.408 mg perindopril, converted in situ to perindopril sodium, and 1.25 mg indapamide.

- 10 mg/2.5 mg strength
  10 mg perindopril tosilate corresponding to 6.816 mg perindopril, converted in situ to perindopril sodium, and 2.5 mg indapamide.

The film-coated tablets are presented in three strengths, which can be distinguished by their shape, dimensions, score line and debossing:

- 2.5 mg/0.625 mg strength
  White, capsule shaped biconvex film-coated tablet are approximately 4 mm width and 8 mm length, debossed with a breakline on one side and plain on the other side. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.
- 5 mg/1.25 mg strength
  White, capsule shaped biconvex film-coated tablet are approximately 5 mm width and 10 mm length, debossed with "P", "I" and a breakline on one side and plain on the other side. The tablet can be divided into equal doses.
- 10 mg/2.5 mg strength
  White, round and biconvex film-coated tablet are approximately 10 mm diameter and plain on both sides.

The excipients are:
Core: - lactose monohydrate, maize starch, sodium hydrogen carbonate (E500 (ii)), pregelatinised starch, (maize), povidone K30 (E1201) and magnesium stearate (E470b)
Film-coating: - *p*oly(vinyl alcohol) - part. hydrolized (E1203), titanium dioxide (E171), macrogol/PEG 3350 (E1521) and talc (E553b)

The tablet cores of the three strengths are dose proportional.

The film-coated tablets are packed in polypropylene (PP) containers with polyethylene (PE) stopper with desiccant.

II.2 Drug Substance

The active substances are perindopril tosilate and indapamide. Perindopril tosilate is not described in the European Pharmacopoeia (Ph.Eur.). Perindopril tosilate is very soluble in water between pH 1.2 to 6.8, methanol, ethanol, acetonitrile and dichloromethane, freely soluble in ethyl acetate, practically insoluble in n-hexane and soluble in water. The substance is present in amorphous form and is hygroscopic. The perindopril tosilate corresponds to the S, S, S, S, S enantiomer.
Indapamide is an established active substance described in the Ph.Eur. Indapamide is practically insoluble in water, and soluble in ethanol. It is a chiral substance which is present as a racemate.

For the drug substance perindopril tosilate, the Active Substance Master File (ASMF) procedure is used. The main objective of the ASMF procedure, commonly known as the European Drug Master File (EDMF) procedure, is to allow valuable confidential intellectual

property or 'know-how' of the manufacturer of the active substance (ASM) to be protected, while at the same time allowing the applicant or marketing authorisation holder (MAH) to take full responsibility for the medicinal product, the quality and quality control of the active substance. Competent Authorities/EMA thus have access to the complete information that is necessary to evaluate the suitability of the use of the active substance in the medicinal product.

For the active substance indapamide, the CEP procedure is used. Under the official Certification Procedures of the EDQM of the Council of Europe, manufacturers or suppliers of substances for pharmaceutical use can apply for a certificate of suitability concerning the control of the chemical purity and microbiological quality of their substance according to the corresponding specific monograph, or the evaluation of reduction of Transmissible Spongiform Encephalopathy (TSE) risk, according to the general monograph, or both. This procedure is meant to ensure that the quality of substances is guaranteed and that these substances comply with the Ph.Eur.

Manufacturing process

Perindopril tosilate

The manufacturing process consists of a one-step synthesis. Adequate specifications have been adopted for starting materials, solvents and reagents. The active substance has been adequately characterised and the manufacturing process is described in sufficient detail.

Indapamide

A CEP has been submitted; therefore no details on the manufacturing process have been included.

Quality control of drug substance

Perindopril tosilate

The drug substance in-house specification is considered adequate to control the quality. Batch analytical data demonstrating compliance with this specification have been provided for three commercial scale batches.

Indapamide

The drug substance specification is considered adequate to control the quality and meets the requirements of the monograph in the Ph.Eur. Batch analytical data demonstrating compliance with this specification have been provided for nine batches tested by the active substance manufacturer and seven batches tested by the drug product manufacturer.

Stability of drug substance

Perindopril tosilate

Stability data have been provided for seventeen commercial scale batches in accordance with applicable European guidelines. Based on the data submitted, a retest period could be granted of 60 months when stored under the stated conditions.

Indapamide

The active substance is stable for five years when stored under the stated conditions. Assessment thereof was part of granting the CEP (and has been granted by the EDQM).

II.3 Medicinal Product

Pharmaceutical development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines. The pharmaceutical development has been described into sufficient detail, including a justification for the choice of the less stable amorphous drug substance perindopril tosilate.
Two bioequivalence studies were conducted with the 5 mg/1.25 mg and 10 mg/2.5 mg strengths. Sufficient information has been provided on the development of the comparative dissolution method and its discriminatory power has been demonstrated.
The tablets of the 2.5 mg/0.625 mg and 5 mg/1.25 mg strengths contain a score line. As breaking of the tablets of the 2.5 mg/0.625 mg results in a strength that is not included in the posology in the product information, the score line of this strength can only be used to facilitate breaking for ease of swallowing. The functionality of the score line of the tablets of the 5 mg/1.25 mg strength has been demonstrated according to the Ph.Eur.

Manufacturing process

The manufacturing process has been validated according to relevant European/ICH guidelines. The manufacturing process is considered a non-standard process, as the content of indapamide in the tablets is less than 2%. The process involves blending, wet granulation, compression, and coating with a non-functional film-coat. A common blend is used for all strengths. The manufacturing process has been described in sufficient detail. Process validation data on the product have been presented for three full batches per strength, in accordance with the relevant European guidelines.

Control of excipients

All excipients and all ingredients of the coating agent comply with the European Pharmacopoeia. These specifications are acceptable.

Quality control of drug product

The finished product specifications are adequate to control the relevant parameters for the dosage form. The specification includes tests for description, identification of the active substances and colouring agent titanium dioxide, uniformity of dosage units by mass variation, subdivision of tablets (5 mg/1.25 mg strength only), dissolution, assay, impurities/degradation products, one specific indapamide impurity and microbiological quality. Friability, resistance to crushing, core weight and tablet weight are tested in process. Limits in the specification have been justified and are considered appropriate for adequate quality control of the product. The in-house analytical methods have been adequately described and validated.
An adequate nitrosamines risk evaluation report has been provided and revealed risks for N-nitroso perindopril originating from perindopril tosilate and N-nitrosodiethylamine (NDAE), and one specific indapamide impurity originating from indapamide. Confirmatory testing showed that the levels of N-nitroso perindopril, NDEA and the indapamide impurity are sufficiently low to omit a test in the drug product specification.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data of three pilot and three commercial scale batches of each strength from the proposed production site have been provided, demonstrating compliance with the release specification.

Stability of drug product

Stability studies of the drug product included three pilot and three commercial scale batches of the 2.5 mg/0.625 mg and 5 mg/1.25 mg strengths and three commercial scale batches of the 10 mg/2.5 mg strength. The batches were stored at 25°C/ 60% RH (36 months) and 40°C/75% RH (6 months) in accordance with applicable European guidelines. Photostability data results were within specification limits, demonstrating that the unprotected tablets are not sensitive to light. On basis of the data submitted, a shelf life was granted of 28 months. The labelled storage conditions are 'Keep the container tightly closed in order to protect from moisture'.

In-use stability data have been provided demonstrating that the product remains stable for 28 months following first opening of the container.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies

Scientific data and/or certificates of suitability issued by the EDQM for lactose have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via medicinal products has been satisfactorily demonstrated. Magnesium stearate is of vegetable origin.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Perindopril tosilaat/Indapamide DOC has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.

No post-approval commitments were made.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

Since Perindopril tosilaat/Indapamide DOC is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment was therefore not deemed necessary.

III.2 Discussion on the non-clinical aspects

This product is a generic formulation of Preterian which is available on the European market. Reference was made to the preclinical data obtained with the innovator product. A non-

clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which was based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. Therefore, the member states agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Introduction

Perindopril tosilate and indapamide are well-known active substances with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The member states agreed that no further clinical studies are required, besides the two bioequivalence studies, which are discussed below. For the 2.5 mg/0.625 mg strength, a biowaiver of strengths is requested.

IV.2 Pharmacokinetics

The MAH conducted two bioequivalence studies in which the pharmacokinetic profile of the test product Perindopril tosilaat/Indapamide DOC 5 mg/1.25 mg (DOC Generici S.r.l., Italy) was compared with the pharmacokinetic profile of the originator product BiPreterax N, 5/1.25 mg film-coated tablets (Les Laboratoires Servier Industrie, Germany), and the test product Perindopril tosilaat/Indapamide DOC 10 mg/2.5 mg, film-coated tablets (DOC Generici S.r.l., Italy) was compared with the pharmacokinetic profile of the originator product Noliterax 10/2.5 mg film-coated tablets (Les Laboratoires Servier Industrie, Hungary).

The choice of the reference product in the bioequivalence studies has been justified by comparison of dissolution study results and composition. The formula and preparation of the bioequivalence batches (biobatch) was identical to the formula proposed for marketing. The biobatches are acceptable from a chemical-pharmaceutical point of view. The comparative dissolution profiles of the biobatches do not fully support bioequivalence. An acceptable justification has been provided for the differences seen between the test and reference product at pH 6.8.

<u>Biowaiver</u>
The following general requirements were met for the waiver for additional strength, according to the EMA Bioequivalence guideline:

a. All strengths are manufactured by the same process.
b. The qualitative composition of the different strengths is the same.
c. The composition of the strengths is quantitatively proportional, i.e. the ratio between the amount of each excipient to the amount of active substance(s) is the same for all strengths.
d. The comparative dissolution profiles of the three strengths are similar *in vitro* at three pH values (pH 1.2, pH 4.5 and pH 6.8). For perindopril more than 85% of the

drug is dissolved within 15 minutes, hence the dissolution profiles can be accepted as similar without further mathematical evaluation. For indapamide, less than 85% of the drug is dissolved within 15 minutes. Therefore, dissolution similarity is determined using the f_2 calculations. The f_2 values are 64, 74, and 72% in case of pH 1.2, 4.5 and 6.8, respectively, demonstrating similarity of profiles for indapamide. An f_2 value between 50 and 100% suggests that the dissolution profiles are similar.

As all of the conditions for a biowaiver for additional strengths are met, a biowaiver for Perindopril tosilate 2.5mg/0.625mg film-coated tablets is justified.

Bioequivalence studies

Study 1, with perindopril/indapamide 5 mg/1.25 mg under fasting conditions

Design

An open label, single-dose, randomised, two-period, two-treatment, 2-way crossover bioequivalence study was carried out under fasted conditions in 36 healthy (28 male and 8 female) subjects, aged 24-55 years. Each subject received a single dose (perindopril/indapamide 5 mg/1.25 mg) of one of the two perindopril/indapamide formulations in each period, according to the randomisation scheme. The tablet was administered orally with 240 ml water after an overnight fast of at least 10 hours prior to drug administration. There were two dosing periods, separated by a washout period of 22 days.

For perindopril, blood samples were collected pre-dose and at 0.25, 0.5, 0.75, 1, 1.25, 1.5, 2, 3, 4, 5, 6, 8 and 12 hours after administration of the products.
For indapamide, blood samples were collected pre-dose and at 0.25, 0.5, 0.75, 1, 1.25, 1.5, 1.75, 2, 2.25, 2.5, 2.75, 3, 4, 6, 8, 12, 24, 36, 48, and 72 hours after administration of the products.

The design of the study is acceptable.

Analytical/statistical methods

The analytical method has been adequately validated and is considered acceptable for analysis of the plasma samples. The methods used in this study for the pharmacokinetic calculations and statistical evaluation are considered acceptable.

Results

36 Subjects were enrolled. Three subjects were withdrawn or withdrew from the study prior to Period II: one was withdrawn due to a positive cotinine test and two subjects withdraw for personal reasons. No serious adverse events (SAEs) were observed. In total, 33 subjects were eligible for pharmacokinetic analysis.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} (median, range)) of perindopril/indapamide, 5 mg/1.25 mg under fasted conditions.

Treatment N=33		**AUC_{0-t} (pg.h/mL)**	**$AUC_{0-\infty}$ (pg.h/mL)**	**C_{max} (pg/mL)**	**t_{max} (h)**
perindopril	**Test**	46448 ± 7704	47083 ± 7708	42449 ± 8982	0.75 (0.25 - 1.25)
	Reference (BiPreterax N)	44505 ± 8629	45186 ± 8605	40688 ± 9791	0.75 (0.500 - 1.00)
	***Ratio (90% CI)**	1.05 (1.01 - 1.09)	1.05 (1.01 - 1.09)	1.05 (0.98 – 1.12)	--
Treatment N=33		**AUC_{0-t} (ng.h/mL)**	**$AUC_{0-\infty}$ (ng.h/mL)**	**C_{max} (ng/mL)**	**t_{max} (h)**
indapamide	**Test**	974 ± 186	1007 ± 201	60 ± 11	1.00 (0.75 - 4.00)
	Reference (BiPreterax N)	933 ± 173	964 ± 186	54 ± 10.0	1.50 (1.00 - 4.00)
	***Ratio (90% CI)**	1.04 1.02 – 1.07	1.04 1.02 – 1.07	1.11 (1.07 – 1.15)	--

$AUC_{0-\infty}$	Area under the (plasma) concentration-time curve from time zero to infinity
AUC_{0-t}	Area under the (plasma) concentration-time curve from time zero to the last quantifiable concentration
C_{max}	Maximum (plasma) concentration
t_{max}	Time after administration when maximum (plasma) concentration occurs
CI	Confidence interval

**In-transformed values*

Study 2, with perindopril/indapamide <u>10 mg/2.5 mg</u> under fasting conditions

Design

A single-dose, randomised, two-period, two-treatment, two-way crossover bioequivalence study was carried out under fasted conditions in 32 healthy (24 male and 8 female) subjects, aged 22-54 years. Each subject received a single dose (10 mg/2.5 mg) of one of the two perindopril/indapamide formulations in each period, according to the randomisation scheme. The tablet was administered orally with 240 ml water after an overnight fast of at least 10 hours. There were two dosing periods, separated by a washout period of 21 days.

For perindopril and perindoprilat (active form of the prodrug perindopril, conversion takes place in the liver), blood samples were collected pre-dose and at 0.5, 1, 1.5, 2, 2.5, 3, 4, 6 and 8 hours after drug administration.
For perindopril only, additional blood samples were collected at 0.167, 0.333, 0.667, 0.833, and 1.25 hours after drug administration.
For perindoprilat only, additional blood samples were collected at 3.5, 4.5, 5, 12, 24, 48 and 72 hours after drug administration.
For indapamide, blood samples were collected in each period pre-dose and at 0.333, 0.667, 0.833, 1, 1.25, 1.5, 1.75, 2, 2.5, 3, 4, 6, 8, 12, 24, 48 and 72 hours after drug administration.

The design of the study is acceptable.

Analytical/statistical methods
The analytical method has been adequately validated and is considered acceptable for analysis of the plasma samples. The methods used in this study for the pharmacokinetic calculations and statistical evaluation are considered acceptable.

Results
32 Subjects enrolled in the study. One subject was withdrawn prior to Period II due to an adverse event (urticaria). The safety of the subject was not at risk. The AE was mild in severity and considered not related with the study medication. In total, 31 subjects were eligible for pharmacokinetic analysis.

Table 2. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} (median, range)) of perindopril/indapamide, 10 mg/2.5 mg under fasted conditions.

Treatment N=31		**AUC_{0-t} (pg.h/mL)**	**$AUC_{0-\infty}$ (pg.h/mL)**	**C_{max} (pg/mL)**	**t_{max} (h)**
perindopril	**Test**	89740 ± 18654	90810 ± 18487	72955 ± 19186	0.8 (0.5 - 1.3)
	Reference (Noliterax)	85066 ± 16483	86059 ± 16470	76524 ± 21598	0.7 (0.5 – 2.0)
	***Ratio (90% CI)**	1.06 (1.02 – 1.09)	1.06 (1.02 – 1.09)	0.96 (0.88 – 1.05)	
Treatment N=31		**AUC_{0-t} (ng.h/mL)**	**$AUC_{0-\infty}$ (ng.h/mL)**	**C_{max} (ng/mL)**	**t_{max} (h)**
indapamide	**Test**	2010 ± 434	2074 ± 471	118 ± 23	1.5 (0.7 – 6.0)
	Reference (Noliterax)	1886 ± 458	1949 ± 504	104 ± 23	1.6 (0.7 – 6.0)
	***Ratio (90% CI)**	1.08 (1.06 – 1.09)	1.07 (1.06 – 1.09)	1.14 (1.09 – 1.20)	--

$AUC_{0-\infty}$ Area under the (plasma) concentration-time curve from time zero to infinity
AUC_{0-t} Area under the (plasma) concentration-time curve from time zero to the last quantifiable concentration
C_{max} Maximum (plasma) concentration
t_{max} Time after administration when maximum (plasma) concentration occurs
CI Confidence interval

**ln-transformed values*

Conclusion on bioequivalence studies:
The 90% confidence intervals calculated for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max} of both perindopril and indapamide are within the bioequivalence acceptance range of 0.80 – 1.25. Based on the submitted bioequivalence studies Perindopril tosilaat/Indapamide DOC 5 mg/1.25 mg and 10 mg/2.5 mg, film-coated tablets is considered bioequivalent with Preterian, film-coated tablets. With respect to safety of the test formulations in both bioequivalence studies, no peculiarities with respect to adverse events were observed.

The results of the BE study with the 5 mg/1.25 mg formulation can be extrapolated to the 2.5 mg/0.625 mg strength, according to conditions in Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1/Corr*, section 4.1.6.

The MEB has been assured that the bioequivalence study has been conducted in accordance with acceptable standards of Good Clinical Practice (GCP, see Directive 2005/28/EC) and Good Laboratory Practice (GLP, see Directives 2004/9/EC and 2004/10/EC).

IV.3 Risk Management Plan

The 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 Perindopril tosilaat/Indapamide DOC. At the time of approval, the most recent version of the RMP was version 0.2 signed 17 July 2022.

Table 3. Summary table of safety concerns as approved in RMP

Important identified risks	None
Important potential risks	None
Missing information	None

The member states agreed that routine pharmacovigilance activities and routine risk minimisation measures are sufficient for the risks and areas of missing information.

IV.4 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Preterian. The MAH demonstrated through two bioequivalence studies that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of this reference product. Risk management is adequately addressed. This generic medicinal product can be used instead of the reference product.

V. USER CONSULTATION

A user consultation with target patient groups on the package leaflet (PL) has been performed on the basis of a bridging report making reference to Perindopril/Indapamide Teva 10 mg/2.5 mg film-coated tablets, NL/H/3522/001/DC. Differences in key safety messages are justified making reference to the PLs of Coversyl Plus arg (for the 10 mg/2.5 mg dosage, procedure nr. FR/H/0345 and for the 2.5 mg/0.625 mg and 5 mg/1.25 mg dosages, procedure nr FR/H/0130). The bridging report submitted by the MAH has been found acceptable; bridging is justified for both content and layout of the leaflet.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Perindopril tosilaat/Indapamide DOC 2.5 mg/0.625 mg, 5 mg/1.25 mg and 10 mg/2.5 mg, film-coated tablets have a proven chemical-pharmaceutical quality and are generic forms of Preterian 2.5 mg/0.625 mg, film-coated tablets. Preterian is a well-known medicinal product with an established favourable efficacy and safety profile.

Bioequivalence has been shown to be in compliance with the requirements of European guidance documents.

The Board followed the advice of the assessors.

There was no discussion in the CMD(h). Agreement between member states was reached during a written procedure. The member states, on the basis of the data submitted, considered that essential similarity has been demonstrated for Perindopril tosilaat/Indapamide DOC with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 6 March 2024.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
NL/H/5718/001-3/IB/001/G	Change in the name and/or address of: a manufacturer (including where relevant quality control testing sites); or an ASMF holder; or a supplier of the active substance, starting material, reagent or intermediate used in the manufacture of the active substance (where specified in the technical dossier) where no Ph. Eur. Certificate of Suitability is part of the approved dossier; or a manufacturer of a novel excipient (where specified in the technical dossier) Changes in the manufacturing process of the active substance - Minor change to the restricted part of an Active Substance Master File. Change in the specification parameters and/or limits of the immediate packaging of the active substance - Addition of a new specification parameter to the specification with its corresponding test method	No	1 January 2026	Approved	N.A.-