COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Varenicline Viatris 0.5 mg, 1 mg and 0.5 mg + 1 mg, film-coated tablets (varenicline tartrate)

NL/H/6102/001-003/DC

Date: 1 April 2026

This module reflects the scientific discussion for the approval of Varenicline Viatris 0.5 mg, 1 mg and 0.5 mg + 1 mg, film-coated tablets. The procedure was finalised on 30 May 2025. 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 Varenicline Viatris 0.5 mg, 1 mg and 0.5 mg + 1 mg, film-coated tablets, from Viatris Limited.

The product is indicated for smoking cessation in adults.

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 innovator product Champix 0.5 mg and 1 mg, film-coated tablets, which has been registered in the EEA via a centralised procedure (EU/1/06/360) since 25 September 2006.

The concerned member states (CMS) involved in this procedure were Belgium, Czechia, Denmark, Finland, Germany, Italy, Norway and Portugal.

II. QUALITY ASPECTS

II.1 Introduction

Varenicline Viatris 0.5 mg and 1 mg are film-coated tablets. The tablets are presented in two strengths which can be distinguished by their shape, size and debossing.

Varenicline Viatris 0.5 mg
White to off-white coloured, round shaped, biconvex, film-coated tablets, approximately 6.1 mm in diameter, debossed with “M 33” on one side and plain on other side.
Each tablet contains as active substance 0.5 mg varenicline, as varenicline tartrate.

Varenicline Viatris 1 mg
White to off-white coloured, capsule shaped, biconvex, film-coated tablets, approximately 10.2 mm x 5.2 mm in diameter, debossed with “M 34” on one side and plain on other side.
Each tablet contains as active substance 1 mg varenicline, as varenicline tartrate.

The excipients are:
Tablet core – microcrystalline cellulose, calcium hydrogen phosphate and magnesium stearate.
Tablet coating – HPMC 2910/hypromellose 6 mPas, hydroxypropyl cellulose and titanium dioxide.

The two tablet strengths are dose proportional.

The film-coated tablets are packed in oriented polyamide/Aluminium/polyvinyl chloride (OPA/Aluminium/PVC) blisters with aluminium foil.

II.2 Drug Substance

The active substance is varenicline tartrate, an established active substance not described in the European Pharmacopoeia (Ph.Eur.). Varenicline tartrate is an off-white powder and is soluble in water. For this product a suitable polymorphic form is consistently manufactured.

The Active Substance Master File (ASMF) procedure is used for the active substance. 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.

Manufacturing process

The manufacturing process consists of a six 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.

Quality control of drug substance

The active substance specification is considered adequate to control the quality and meets the in-house requirements of the MAH. Batch analytical data demonstrating compliance with this specification have been provided for three batches.

Stability of drug substance

Stability data on the active substance have been provided for three batches in accordance with applicable European guidelines. Based on the data submitted, a retest period could be granted of 12 months when stored under the stated conditions.

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. A specific varenicline impurity, of special relevance for products containing varenicline as active substance, has been considered for the development of the product. Measurements of this impurity in development have been provided. The choice of excipients is justified and their functions explained.

Manufacturing process

The manufacturing process is common and the control strategy is sufficient to ensure the manufacturing of an homogenous product. Process validation data on the product have been

presented for three consecutive commercial-size batches for each strength in accordance with the relevant European guidelines.

Control of excipients
The excipients used in the generic product are commonly used for the proposed pharmaceutical form. The quality of the excipients is considered to be properly controlled by the proposed specifications. 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 drug substance, identification of colourant, water, dissolution, uniformity of dosage units, related substances, assay and microbial contamination. Limits in the specification have been justified and are considered appropriate for adequate quality control of the product. An adequate nitrosamines risk evaluation report has been provided. No risk for presence of nitrosamines in the drug product was identified.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data from three commercial-size batches for each strength from the proposed production site have been provided, demonstrating compliance with the specification.

Stability of drug product
Stability data on the product have been provided for three commercial-size batches for each strength stored at 25°C/60% RH (12 months) and 40°C/75% RH (6 months). The stability was tested in accordance with applicable European guidelines. Photostability studies in accordance with ICH GL Q1B were performed and showed that the product is stable when exposed to light. On basis of the data submitted, a shelf life was granted of 24 months. No specific storage conditions needed to be included in the SmPC or on the label.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Varenicline Viatris 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 Varenicline Viatris 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 Champix 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

Varenicline tartrate is a well-known active substance with established efficacy and tolerability. To support the application, the MAH did not submit any clinical trial reports, bioequivalence studies or therapeutic equivalence studies, instead a BCS (Biopharmaceutics Classification System)-based biowaiver was requested.

IV.2 Pharmacokinetics

Biowaiver

The MAH has submitted a justification for a BCS-based biowaiver for Varenicline Viatris 0.5 mg and 1 mg, film-coated tablets with Champix 0.5 mg and1 mg, film-coated tablets as reference product.

Varenicline Viatris 0.5 mg and 1 mg film-coated tablets meet all the requirements for a BCS-based biowaiver:

a. Drug substance varenicline tartrate has been proven to exhibit high solubility and complete absorption (BCS class I)
b. Drug product is an immediate release solid oral pharmaceutical product.
c. Reference and test product do not contain any excipient which might affect the absorption.
d. Dissolution characteristics of the test and reference product have been demonstrated very rapid (> 85 % within 15 min) under prescribed conditions.

The dissolution was investigated according to the EMA Bioequivalence guideline. Based on the submitted data, varenicline can be considered a BSC Class I drug. Comparative dissolution tests showed that test and reference product both dissolved very rapidly in all three media (≥85% in 5 minutes) in dissolution media pH 1.2, pH 4.5 and pH 6.8. The test and reference formulation contain normal excipients and no critical excipients are included. Therefore, the criteria for a BCS-based waiver has been fulfilled for Varenicline Viatris 0.5 mg and 1 mg, film-coated tablets.

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 Varenicline Viatris. At the time of approval, the most recent version of the RMP was version 0.2 dated 26 September 2024.

Table 1. Summary table of safety concerns as approved in RMP

Important identified risks	None
Important potential risks	None
Missing information	• Use in patients with cardiovascular disease (CVD) • Use in pregnancy

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 Champix. No new clinical studies were conducted. The MAH demonstrated through a biowaiver that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of the 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 Duloxetine Mylan 30 mg, hard gastro-resistant tablets, EMEA/H/C/003981 for layout and to Champix 0.5 mg and 1 mg, film-coated tablets, EU/1/06/360 for content. 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

Varenicline Viatris 0.5 mg, 1 mg and 0.5 mg + 1 mg, film-coated tablets have a proven chemical-pharmaceutical quality and are generic forms of Champix 0.5 mg and 1 mg, film-coated tablets. Champix is a well-known medicinal product with an established favourable efficacy and safety profile.

No bioequivalence study has been performed, a biowaiver is claimed and can be granted.

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 Varenicline Viatris with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 30 May 2025.

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/6102/001-3/P/001	The addition of the week number to the inner carton and the optional sun/moon symbols to the immediate packaging (blister foil). Harmonising the product name on outer carton for treatment initiation pack in line with SmPC and Package leaflet. The addition of the week number and 'sun/moon' symbol is proposed to clarify the dosage regimen and to indicate am/pm dose: the week number and the 'sun/moon' symbol has been added to the Labelling text in grey shading	No	31-10-2025	Approved	N.A.