COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Fexofenadine HCl Viatris 120 mg and 180 mg, film-coated tablets (fexofenadine hydrochloride)

NL/H/5769/001-002/DC

Date: 24 February 2026

This module reflects the scientific discussion for the approval of Fexofenadine HCl Viatris 120 mg and 180 mg, film-coated tablets. The procedure was finalised on 4 July 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 Fexofenadine HCl Viatris 120 mg and 180 mg, film-coated tablets, from Viatris Limited.

The 120 mg strength is indicated in adults and children 12 years and older for the relief of symptoms associated with seasonal allergic rhinitis.

The 180 mg strength is indicated in adults and children 12 years and older for the relief of symptoms associated with chronic idiopathic urticaria

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 Telfast 120 mg and 180 mg film-coated tablets (IE/H/0805/002-003) which has been registered in the United Kingdom by Aventis Pharma Limited since 4 December 1996. The current marketing authorisation holder (MAH) is Opella Healthcare UK, trading as Sanofi.
In the Netherlands, Allegra Fexotabs 120 mg omhulde tabletten and Telfast 180 mg film omhulde tabletten have been registered since 27 October 1997 by the national procedures RVG 21624 and RVG 21625. The initial MAH was Sanofi-Aventis Netherlands B.V. The current MAH is Opella Healthcare France.

The concerned member states (CMS) involved in this procedure were Denmark, France, Iceland, Italy, Portugal, Slovakia and Sweden.

II. QUALITY ASPECTS

II.1 Introduction

Fexofenadine HCl Viatris is a peach-coloured capsule shaped film-coated tablet. The two strengths can be distinguished by their appearance, based on size and debossing, as follows:

<u>Fexofenadine HCl Viatris 120 mg</u>
The film-coated tablets are 16 mm x 6.2 mm and are debossed with ‘120’ on one side and ‘FX’ on other side.
Each tablet contains 120 mg fexofenadine hydrochloride, which is equivalent to 112 mg of fexofenadine.

Fexofenadine HCl Viatris 180 mg
The film-coated tablets are 17.1 mm x 7.6 mm and are debossed with '180' on one side and 'FX' on other side.
Each tablet contains 180 mg fexofenadine hydrochloride, which is equivalent to 168 mg of fexofenadine.

The excipients are:
Tablet core - lactose monohydrate, low substituted hydroxypropylcellulose (E463), pregelatinised starch, colloidal anhydrous silica, microcrystalline cellulose (E460), croscarmellose sodium (E468) and magnesium stearate.

Film-coating – hypromellose, povidone, titanium dioxide (E171), iron oxide red (E172), iron oxide yellow (E172), macrogol and colloidal anhydrous silica.

The two tablet strengths are fully dose proportional.

The film-coated tablets are packed in:
- aluminium/polyvinyl chloride/polyvinylidene chloride (Alu/PVC/PVDC) blister packs
- aluminium/polyvinyl chloride/polyethylene/ACLAR (Alu/PVC/PE/ACLAR) blister packs
- HDPE bottles with pp screw cap

II.2 Drug Substance

The active substance is fexofenadine hydrochloride, an established active substance described in the European Pharmacopoeia (Ph.Eur.). The active substance is slightly soluble in water. It shows polymorphism. For this product, polymorphic form I is consistently produced.

Two CEP procedures are used for the active substance. 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
Two CEPs have been submitted; therefore no details on the manufacturing process have been included.

Quality control of drug substance
The active substance specification is considered adequate to control the quality and meets the requirements of the monograph in the Ph.Eur. and requirements of the CEPs, with additional tests for polymorphic identity and particle size distribution. Batch analytical data demonstrating compliance with this specification have been provided for nine batches from active substance manufacturing site I and three batches from site II.

Stability of drug substance
The active substance is stable for 60 months when stored under the stated conditions. Assessment thereof was part of granting the CEPs (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 choice of excipients is justified and their functions explained. The main development studies concerned the characterisation of the reference products, performance of formulation optimisation studies and dissolution method development. The choices of the packaging and manufacturing process are justified. The pharmaceutical development of the product has been adequately performed.

Manufacturing process
The manufacturing process has been validated according to relevant European/ICH guidelines. Process validation data on the product have been presented for at least three full scaled batches per strength in accordance with the relevant European guidelines.

Control of excipients
The excipients comply with Ph.Eur. requirements, except for the iron oxides that comply with the purity criteria of Regulation 231/2012. Functionality-related characteristics are controlled for several of the excipients. 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, identity (drug substance and colourants), average mass, uniformity of mass, disintegration time, dissolution, uniformity of dosage units, related substances, assay, microbial quality, loss on drying and residual isopropyl alcohol. 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 three pilot scaled batches per 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 from six production scaled batches per strength stored at 25°C/60% RH (6-36 months) and 40°C/75% RH (6 months) in accordance with applicable European guidelines. Photostability studies were performed in accordance with ICH recommendations and showed that the product is stable when exposed to light. On basis of the data submitted, a shelf life was granted of three years. No specific storage conditions needed to be included in the SmPC or on the label.

Given the overall stability of the drug product, no separate in-use shelf life is needed for the HDPE bottle pack in line with the EMA Q&A on this topic.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
Scientific data and/or certificates of suitability issued by the EDQM for excipient lactose monohydrate 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.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Fexofenadine HCl 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 Fexofenadine HCl 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 Telfast 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

Fexofenadine hydrochloride is a well-known active substance 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 one

bioequivalence study, which is discussed below. In addition, a biowaiver of strength was requested for the 120 mg strength.

IV.2 Pharmacokinetics

The MAH conducted a bioequivalence study in which the pharmacokinetic profile of the test product Fexofenadine HCl Viatris 180 mg, film-coated tablets (Viatris Limited, Ireland) was compared with the pharmacokinetic profile of the reference product Telfast 180 mg film-coated tablets (Sanofi-Aventis Ireland Limited T/A SANOFI, Ireland).

The choice of the reference product in the bioequivalence study has been justified by comparison of dissolution study results and composition. Comparative dissolution testing at three pHs (pH 1.2, 4.5 and 6.8) has been successfully performed in support of the biowaiver for the 120 mg product. The formula and preparation of the bioequivalence batch was identical to the formula proposed for marketing.

Biowaiver

A biowaiver of additional strength for the Fexofenadine HCl Viatris 120 mg, film-coated tablets, based on the bioequivalence study of the 180 mg (according to the EMA Bioequivalence guideline), can be granted as:

a. the two pharmaceutical strengths are manufactured by the same process and manufacturer,
b. the qualitative composition of both strengths is the same,
c. the composition of both strengths are 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 (for immediate release products coating components,
d. the pharmacokinetics of fexofenadine can be considered dose-linear for the 120-180 mg dose range,
e. the dissolution is very rapid (>85% within 15 minutes) for both strengths at pH 1.2, 4.5 and 6.8. No f_2-test is required for dissolution similarity.

Bioequivalence studies

Design

A single-dose, randomised, four-period, two-treatment, two-sequence, fully replicate designed crossover bioequivalence study was carried out under fasted conditions in 44 healthy male subjects, aged 20-43 years. Each subject received a single dose (180 mg) of one of the two fexofenadine hydrochloride formulations. The tablet was orally administered with 240 ml water after an overnight fasting of at least 10 hours. There were four dosing periods, separated by a washout period of seven days.

Blood samples were collected pre-dose and at 0.33, 0.67, 1, 1.33, 1.67, 2, 2.33, 2.67, 3, 3.33, 3.67, 4, 5, 6, 8, 10, 12, 16, 24, 36 and 48 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
During the study, five subjects were withdrawn and six subjects dropped out. For four of the five withdrawn subjects, the reason was an adverse event (vomiting or acute gastroenteritis). Two of the drop-outs did not check-in for period II, III and IV. One subject did not check-in for period II and IV, another subject did not check-in for period II and one subject did not check-in for period III. Another subject withdrew his consent from 10 hours post dose onwards.
The data from 36 subjects were eligible for pharmacokinetic analysis. Out of these subjects, 33 subjects completed all four periods and three subjects completed at least 1 period for the test product and 1 period for the reference product according to the protocol.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} (median, range)) of fexofenadine hydrochloride, 180 mg under fasted conditions.

Treatment N=34-36	**AUC_{0-t}** (ng.h/ml)	**$AUC_{0-\infty}$** (ng.h/ml)	**C_{max}** (ng/ml)	**t_{max}** (h)
Test **(N(T1)=35 / (N(T2)=34)**	4528 ± 1308	4596 ± 1324	682 ± 246	2.33 (0.67-6.00)
Reference **(N(R1)=36 / (N(R2)=35)**	4587 ± 1447	4648 ± 1461	679 ± 297	2.00 (0.67-6.00)
***Ratio** **(90% CI)**	1.00 (0.93-1.07)	1.00 (0.93-1.07)	1.04 (0.95-1.14)	-

$AUC_{0-\infty}$	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 t = 48 hours
C_{max}	Maximum plasma concentration
t_{max}	Time after administration when maximum plasma concentration occurs
CI	Confidence interval

**ln-transformed values*

Conclusion on bioequivalence study:
The 90% confidence intervals calculated for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max} are within the bioequivalence acceptance range of 0.80 – 1.25. Based on the submitted bioequivalence study Fexofenadine HCl Viatris 180 mg is considered bioequivalent with Telfast, 180 mg.

The results of the bioequivalence study with the 180 mg formulation can be extrapolated to the other strength of 120 mg, 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 Fexofenadine HCl Viatris. At the time of approval, the most recent version of the RMP was version 0.2 dated 7 November 2023.

Table 2. 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 Telfast. The MAH demonstrated through a bioequivalence study 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 Fexofenadine Sandoz 120 mg and 180 mg film-coated tablets, NL/H/3619/001-002/DC (for content) and to Duloxetine Mylan 30 mg hard gastro-resistant capsules, EMEA/H/C/003981 (for design/layout). 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

Fexofenadine HCl Viatris 120 mg and 180 mg, film-coated tablets have a proven chemical-pharmaceutical quality and are generic forms of Telfast 120 mg and 180 mg film-coated tablets. Telfast 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 Fexofenadine HCl Viatris with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 4 July 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/5769/002/P/001	Article 61(3): to update the PIL and Labelling	Yes	13-11-2024	Approved	N.A.
NL/H/5769/001-002/IA/001/G	Change in test procedure for active substance or starting material/reagent /intermediate used in the manufacturing process of the active substance - Deletion of a test procedure for the active substance or a starting material/reagent / intermediate, if an alternative test procedure is already authorised. Change in test procedure for active substance or starting material/reagent /intermediate used in the manufacturing process of the active substance - Minor changes to an approved test procedure. Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: For an active substance, For a	No No No	16-2-2026	Approved	N.A.

	starting material/reagent /intermediate used in the manufacturing process of the active substance, For an excipient - European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer. Change in test procedure for the finished product - Minor changes to an approved test procedure.	No			