COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Eletriptan Viatris 20 mg and 40 mg, film-coated tablets

(eletriptan hydrobromide)

NL/H/4584/001-002/DC

Date: 25 June 2025

This module reflects the scientific discussion for the approval of Eletriptan Viatris 20 mg and 40 mg, film-coated tablets. The procedure was finalised in the United Kingdom (UK/H/5351/001-002/DC). After a transfer in 2018, the current RMS is the Netherlands. The report presented below reflects the original procedure at the time of finalisation in the UK and has not been changed or updated since.

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 data on quality, safety and efficacy, the Member States considered that the applications for Eletriptan Viatris 20 mg and 40 mg, film-coated tablets could be approved. The applications were submitted via the Decentralised Procedure, with the UK as Reference Member State (RMS), and Austria, Belgium, Cyprus, Germany, Denmark, Greece, Spain, Finland, France, Iceland, ltaly, Luxembourg, Malta, the Netherlands, No1way, Portugal and Sweden as Concerned Member States (CMS).

These products can only be obtained with a prescription (legal classification POM).

These applications were made under the Decentralised Procedure (DCP), according to Article 10(1) of Directive 2001/83/EC, as amended, claiming to be generic medicinal products of Relpax 20 mg and 40 mg film-coated tablets (PL 00057/0452-0453), which were initially granted marketing authorisations to the same Marketing Authorisation Holder (Pfizer Limited) in the UK on 12 February 2001.

Eletriptan Viatris 20 mg and 40 mg, film-coated tablets are indicated in adults for acute treatment of the headache phase of migraine attacks, with or without: aura. These products contain the active substance eletriptan (as eletriptan hydrobromide), which is a selective serotonin receptor agonist at the vascular 5- HTrn and neuronal 5-HTrn receptors. lt also exhibits high affinity for the 5-HTlF receptor, which may contribute to its anti-migraine mechanism of action.

No new clinical or non-clinical studies were conducted, which is acceptable given that these applications were based on being generic medicinal products of originator products that have been licensed for over 10 years.

The applicant is also the Marketing Authorisation Holder of the reference products (Relpax 20 mg and 40 mg film-coated tablets, PL 00057 /0452-0453) and has confirmed that Eletriptan 20 mg and 40 mg film- coated tablets are identical to the reference products, with the same qualitative and quantitative composition and the same manufacturing sites and processes. As a consequence, a bioavailability study was not required to demonstrate bioequivalence, and none was provided.

The RMS has been assured that acceptable standards of Good Manufacturing Practice are in place for this product type at all sites responsible for the manufacture, assembly and batch release of these products.

The RMS and CMS considered that the applications could be approved at the end of procedure on 03 October 2013. After a subsequent national phase, marketing authorisations were granted in the UK on 30 October 2013.

II. QUALITY ASPECTS

II.1 Introduction

The excipients of the finished product are:

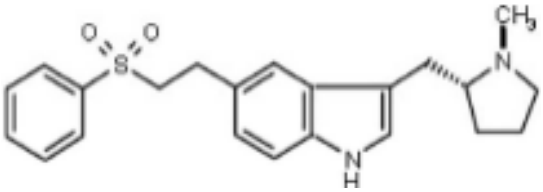
Tablet core:
Microcrystalline cellulose, lactose monohydrate, croscarmellose sodium and magnesium stearate
Film-coating:
Titanium dioxide (E 171), hypromellose, lactose monohydrate, glycerol triacetate and Sunset Yellow FCF Aluminium Lake (El 10).

The finished product is packaged in opaque polyvinylchloride (PVC)/aclar/aluminium blisters in pack sizes of 2, 3, 4, 6, 10, 18, 30 and 100 tablets.

The Marketing Authorisation Holder has stated that not all pack sizes are intended for marketing. However, they have committed to providing the relevant licensing authority with the mock-ups for any pack size before marketing it in that country.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

II.2 Drug Substance

rINN:	Eleptriptan
Chemical name:	(R)-3-(1-methyl-2-pyrrolidinylmethyl)-5-[2-(phenylsulfonyl)ethyl]-lH-indole hydrobromide
Structure:	
Molecular formula:	$C_{22}H_{27}BrN_2O_2S$
Molecular weight:	463.43
Appearance:	White to off-white solid
Solubility:	Slightly soluble in water and aqueous buffers at pH 8 and below, sparingly soluble in acetonitrile and soluble in methanol

Manufacturing process
Synthesis of the drug substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

Quality control of drug substance
An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfacto1y for ensuring compliance with the specification. Satisfactory Certificates of Analysis have been provided for all working standards. Batch analysis data are provided that comply with the specification.

Suitable specifications have been provided for all packaging used. The primary packaging has been shown to comply with current guidelines concerning contact with food.

Stability of drug substance
Appropriate stability data have been generated supporting a suitable retest period when stored in proposed packaging.

II.3 Medicinal Product

Pharmaceutical development
The objective of the development programme was to formulate globally acceptable and stable products that could be considered generic medicinal products. of the currently licensed products Relpax 20 mg and 40 mg film-coated tablets (PL 00057 /0452-0453).

A satisfactory account of the pharmaceutical development has been provided.

Manufacturing process
Satisfactory batch formulae have been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. Suitable in-process controls are in place to ensure the quality of the finished product.

Process validation has been carried out on two commercial-scale batches of each strength of finished product. The results are satisfactory.

Control of excipients
With the exception of the Sunset Yellow FCF Aluminium Lake (E 110), all excipients used comply with their respective European Pharmacopoeia monographs. Sunset Yellow FCF Aluminium Lake (El 10) complies with a suitable in-house specification and is in compliance with current EU Directives concerning the use of colouring agents.

With the exception of the lactose monohydrate, none of the excipients are sourced from animal or human origin. No genetically modified organisms (GMO) have been used in the preparation of this product.

The milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption.

Quality control of drug product

The finished product specifications proposed are acceptable. Test methods have been described that have been adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for all working standards used.

Stability of drug product

Stability studies were performed, in accordance with current guidelines, on batches of finished product manufactured by the finished product manufacturer and packed in the packaging proposed for marketing. The results from these studies support a :shelf-life of 3 years with no special storage conditions.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

As the pharmacodynamic, pharmacokinetic and toxicological properties of eletriptan hydrobromide are well-known, no further non-clinical studies are required and none have been provided.

The applicant's non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the product's pharmacology and toxicology.

Suitable justification has been provided for the non-submission of an environmental risk assessment. As this product is intended for generic substitution with products that are currently marketed, no increase in environmental burden is expected.

III.2 Discussion on the non-clinical aspects

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

IV. CLINICAL ASPECTS

IV.1 Introduction

As Eletriptan Viatris 20 mg and 40 mg, film-coated tablets are identical to the reference products, with the same qualitative and quantitative composition and the same manufacturing sites and processes, bioavailability studies were not required to demonstrate bioequivalence, and none were provided.

IV.2 Pharmacokinetics

No new pharmacokinetic or pharmacodynamic data were submitted with these applications and none were required. The applicant is also the Marketing Authorisation Holder of the

reference products (Relpax 20 mg and 40 mg film-coated tablets, PL 00057 /0452-0453) and has confirmed that Eletriptan Viatris 20 mg and 40 mg, film-coated tablets are identical to the reference products, with the same qualitative and quantitative composition and the same manufacturing sites and processes.

IV.3 Efficacy

No new data on efficacy have been submitted and none are required for this type of application.

IV.4 Safety

No new data on safety have been submitted and none are required for this type of application.

IV.5 SmPC, PIL and Labels

The SmPCs, PILs and text versions of the labels are acceptable from a clinical perspective.

IV.6 Pharmacovigilance System and Risk Management Plan

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 has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

A suitable risk management plan has been provided for these products.

IV.7 Clinical Expert Report and Conclusion

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

The grant of Marketing Authorisations is recommended.

V. USER CONSULTATION

The results of consultations with target patient groups ('user testing'), in accordance with Article 59 of Council Directive 2001/83/EC (as amended) for the package leaflet for the reference products was provided. 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 it contains. As the PILs for Eletriptan Viatris 20 mg and 40 mg, film-coated tablets are consistent with the

approved PIL for Relpax 20 mg and 40 mg film-coated tablets (PL 00057 /0452- 0453) in their content and layout, additional readability testing is not deemed necessary.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The important quality characteristics of Eletriptan Viatris 20 mg and 40 mg, film-coated 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 this type.

CLINICAL
As the applicant for Eletriptan Viatris20 mg and 40 mg, film-coated tablets is the same as the Marketing Authorisation Holder for the reference products and the products are identical, bioavailability studies were not required to demonstrate bioequivalence, and none were provided.

No new clinical data were submitted and none are required for applications of this type.

No new or unexpected safety concerns arose from these applications.

The SmPCs, PILS and text versions of labelling are satisfactory and consistent with those for the reference products.

BENEFIT-RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with eletriptan hydrobromide is considered to have demonstrated the therapeutic value of the compound. The benefit-risk assessment is, therefore, considered to be positive.

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
UK/H/5351/1-2/II/001	To amend section 5.1 (Pharmacodynamics) of the SmPC to more accurately reflect the number of trials and subjects used in the development programme	Yes	4 June 2014	Approved	N.A.
NL/H/4584/1-2/IA/011/G	Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack Change within the range of the currently approved pack sizes + Change in supplier of packaging components or devices (when mentioned in the dossier) Replacement or addition of a supplier	Yes No	20 February 2019	Approved	N.A.
NL/H/4584/1-2/WS/012	Update of the SmPC, PIL and Outer Labels by adding language around sodium as per the Commission excipient guidelines (EMA/CHMP/302620/2017 and EMA/25090/2002 rev.20*) and further minor editorial updates. + Aligning of SmPCs, PILs and Outer Labels to the latest version of the QRD template (MRP version 4.1)	Yes	28 January 2021	Approved	N.A.
NL/H/4584/1-2/WS/013	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	10 January 2021	Approved	N.A.
NL/H/4584/1-2/IB/014	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	11 May 2021	Approved	N.A.
NL/H/4584/1-2/WS/015	Replacement or addition of a manufacturing site for part or all of the manufacturing	No	13 May 2021	Approved	N.A.

	process of the finished product Secondary packaging site				
NL/H/4584/1-2/IA/016/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)	No	2 June 2021	Approved	N.A.
NL/H/4584/1-2/WS/017	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	23 August 2021	Approved	N.A.
NL/H/4584/1-2/WS/018	Change in the name and/or address of the marketing authorisation holder + Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes Yes	6 August 2021	Approved	N.A.
NL/H/4584/1-2/WS/020	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	14 February 2022	Approved	N.A.
NL/H/4584/1-2/IA/021/G	Deletion of manufacturing sites for an active substance, intermediate or finished product, packaging site, manufacturer responsible for batch release, site where batch control takes place, or supplier of a starting material, reagent or excipient (when mentioned in the dossier)*	Yes	30 June 2022	Approved	N.A.
NL/H/4584/1-2/IA/022/G	Change in the name and/or address of the marketing authorisation holder	Yes	18 August 2022	Approved	N.A.
NL/H/4584/1-2/WS/023	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	17 January 2024	Approved	N.A.

NL/H/4584/1-2/IA/024	Change or addition of imprints, bossing or other markings including replacement, or addition of inks used for product marking. Changes in imprints, bossing or other markings	Yes	4 March 2024	Approved	N.A.
NL/H/4584/1-2/WS/025	Change in the manufacturer of a starting material/reagent/intermediate used in the manufacturing process of the active substance or change in the manufacturer (including where relevant quality control testing sites) of the active substance, where no Ph. Eur. Certificate of Suitability is part of the approved dossier Introduction of a new manufacturer of the active substance that is not supported by an ASMF and requires significant update to the relevant active substance section of the dossier	No	6 February 2025	Approved	N.A.

ANNEX 1 - VARIATION ASSESSMENT REPORT
UK/H/5351/1-2/II/001

Recommendation

Based on the review of the data the RMS considers that the va1iation to amend section 5.1 of the SmPCs for Eletriptan Viatris 20 mg film-coated tablets and Eletriptan Viatris 40 mg, film-coated tablets could be approved.

Summary of Product Characteristics

Section 4.8 of the SmPC correctly states:

"Eletriptan has been administered in clinical trials to over 5000 subjects, taking one or two doses of Eletriptan 20 or 40 or 80 mg."

However, some subjects took part in more than one study and individuals were counted once for each study in which they pa1ticipated. To reflect this it is proposed to amend the current SmPC text from:

"The efficacy of Eletriptan in the acute treatment of migraine has been evaluated in 10 placebo-controlled trials that included about 5000 patients who received Eletriptan at doses of 20 to 80 mg."

To:

"The efficacy and safety of eletriptan in the acute treatment of migraine has been evaluated in 10 placebo-controlled trials involving more than 6000 patients (all treatment groups) who received eletiiptan at doses of 20 to 80 mg."

Package leaflet and user test

The proposed changes do not impact on the package leaflet.

Labelling

The proposed changes do not impact on the product labelling.

Overall conclusion

This variation is approvable as the changes are clear and aid the healthcare professional by accurately reflecting the number of trials and subjects used in the development pro gramme.