LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

# Public Assessment Report

# Scientific discussion

# Eletriptan Orion
# (eletriptan hydrobromide)

# SE/H/1743/01-02/DC
# 2017-1068

**This module reflects the scientific discussion for the approval of Eletriptan Orion. The procedure was finalised on 2018-06-29. For information on changes after this date please refer to the module 'Update'.**

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# I. INTRODUCTION

The application for Eletriptan Orion, 20 mg and 40 mg, film-coated tablets, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Orion Corporation, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK, FI and NO as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Relpax, 20 mg and 40 mg, film-coated tablets authorised in UK since 2001, with Pfizer Limited, as marketing authorisation holder.

The reference product used in the bioequivalence study is Relpax, 40 mg, film-coated tablets from Spain with Pfizer S.L. as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83 and conditions to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

# II. QUALITY ASPECTS

## II.1 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.

## II.2 Medicinal 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. NON-CLINICAL ASPECTS

## III.1 Discussion on the non-clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to preclinical data, no further such data have been submitted or are considered necessary.

# IV. CLINICAL ASPECTS

## IV.1 Pharmacokinetics

Bioequivalence was evaluated in one single-dose, two-way crossover study conducted in 36 healthy volunteers, comparing Eletriptan Orion, 40 mg, tablet with Relpax, 40 mg, tablet under fasting conditions. The study was conducted between 22/02/17 and 04/03/17. Blood samples were collected pre-dose and up to 24 hours post-dose. The study design is considered acceptable. Plasma concentrations of eletriptan were determined with an adequately validated LC/MS/MS method.
The results are presented below.

**Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, $t_{max}$ median, range) for eletriptan, n=30.**

| Treatment | $AUC_{0-t}$ ng*h/ml | $C_{max}$ ng/ml | $t_{max}$ h |
|---|---|---|---|
| **Test** | **1133.40±381.13** | **156.91±51.55** | **1.00 0.50-4.00** |
| **Reference** | **1123.22±338.70** | **163.64±51.16** | **0.88 0.50-4.00** |
| ***Ratio (90% CI)** | **100.10 (95.47-104.95)** | **94.86 (87.28-103.09)** | **-** |

$AUC_{0-t}$ 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 $AUC_{0-t}$ and $C_{max}$ the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%. Thus based on the submitted bioequivalence study, Eletriptan Orion 40 mg tablet is considered bioequivalent with Relpax 40 mg tablet.

From a pharmacokinetic point of view, it is sufficient to establish bioequivalence with only one strength as the pharmacokinetics of eletriptan is linear between 20 and 40 mg. The highest strength of 40 mg has been studied which is in accordance with guideline recommendations for drugs with linear pharmacokinetics. The results of study 381-14 with the 40 mg formulation

can be extrapolated to other strength of 20 mg, since all conditions for biowaiver of additional strength are fulfilled.

The pharmacokinetic documentation is considered sufficient.

## IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to clinical efficacy/safety data, no further such data have been submitted or are considered necessary.

## 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 Eletriptan Orion.

Safety specification

| **List of important risks and missing information** | |
|---|---|
| Important identified risks | Myocardial ischaemia or infarction |
| Important potential risks | N/A |
| Missing information | N/A |

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

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

Summary of the RMP
The MAH has satisfactorily responded to the questions raised and updated the RMP accordingly.
**Issue is resolved**
The submitted Risk Management Plan, version 1.1 signed 15-02-2018 is considered acceptable.

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.

# V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to the products Relpax, UK/H/5351/001-002/DC (content) and Venlafaxin Orion, DE/H/1420/01-03/DC (layout). The bridging report submitted by the applicant has been found acceptable.

# VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Eletriptan Orion, is found adequate. There are no objections to approval of Eletriptan Orion, 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 application is therefore recommended for approval.

**List of recommendations not falling under Article 21a/22 of Directive 2001/83 in case of a positive benefit risk assessment**

N/A

**List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC**

N/A

# VII. APPROVAL

The Mutual recognition/Decentralised procedure for Eletriptan Orion, 20 mg and 40 mg, film-coated tablets was positively finalised on 2018-06-29.

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# Public Assessment Report – Update

| Procedure number* | Scope | Product Information affected | Date of end of procedure | Approval/ non approval | Summary/ Justification for refuse |
|---|---|---|---|---|---|
| | | | | | |

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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