LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Sumatriptan Matrix
(sumatriptansuccinat)

Asp no: 2017-0454

This module reflects the scientific discussion for the approval of Sumatriptan Matrix. The procedure was finalised on 2018-03-12. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Sumatriptan Matrix, 50 mg, film-coated tablet, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Matrix Pharmaceuticals A/S, apply for a marketing authorisation in Sweden through a National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is, Imigran Novum, 50 mg, film-coated tablet authorised in Sweden since 2004, with GlaxoSmithKline AB as marketing authorisation holder.

The reference product used in the bioequivalence study is Imigran, 100 mg, film-coated tablet from UK with GlaxoSmithKline 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/EC 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

Sumatriptan has an oral bioavailability of about 15 %. Following an oral dose of sumatriptan maximal plasma concentrations occur at approximately 2 hours. Concomitant intake with a high-fat meal increases the C_{max} by 15% but there are no restrictions with respect to food in the SmPC of the originator.The pharmacokinetics of sumatriptan is linear over the dose range 25-200 mg. The terminal half-life is about 2 hours.

Bioequivalence was evaluated in one single-dose, two-way crossover study conducted in 56 healthy volunteers, comparing sumatriptan, 100 mg, tablets with Imigran, 100 mg, tablets under fasting conditions. The 100 mg strength is not included in the current application. The study was conducted at Accutest Research Laboratories, Navi Mumbai, India between 9th and 31st October 2005. Blood samples were collected pre-dose and up to 24 hours post-dose. The study design is considered acceptable. Plasma concentrations of sumatriptan were determined with a validated LC/MS/MS method. The absence of ISR data has been sufficiently justified. 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%.

Table 1: Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} median, range) for sumatriptan, n=53.

Treatment	AUC_{0-t} ng*h/ml	C_{max} ng/ml	t_{max} h
Test	**358.54±139.01**	**81.22±31.77**	**2.50 (0.50-5.00)**
Reference	**358.99±153.58**	**86.97±34.26**	**3.00 (0.50-5.00)**
***Ratio (90% CI)**	**101.05 (94.62-107.92)**	**93.12 (86.31-100.47)**	**-**

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*

From a pharmacokinetic point of view, absence of studies with the 50 mg strength applied for in this application is acceptable, as the pharmacokinetics of sumatriptan is linear between 25 mg and 200 mg.

Based on the submitted bioequivalence study, Sumatriptan Matrix is considered bioequivalent with Imigran.

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 Sumatriptan Matrix.

Safety specification

Table 1. Summary of safety concerns

Summary of safety concerns	
Important identified risks	• Use in patients with hepatic impairment. • Myocardial ischemia/infarction
Important potential risks	• Use in patients with renal impairment • Cerebrovascular events
Missing information	• Use in pregnancy and lactation • Use in children < 12 years of age

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 submitted Risk Management Plan, version 1.0 signed 7th April, 2017 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 MPA;
- 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 (PL) has been performed on the basis of a bridging report making reference to Sumatriptan Apofri 50 mg, film-coated tablet, NL/H/2279/001-002/DC (content) and Ranitidin Apofri 150 mg film-coated tablet, Dnr 111:2012/79828 (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 products, Sumatriptan Matrix, are found adequate. There are no objections to approval of Sumatriptan Matrix, 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/EC 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

Sumatriptan Matrix, 50 mg, film-coated tablet was approved in the national procedure on 2018-03-12.

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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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