Public Assessment Report
Scientific discussion

Rupatadine Trombicor 10 mg tablets

Rupatadine Fumarate

ES/H/0419/001/DC

Applicant: J. Uriach y Compañía,S. A.

This module reflects the scientific discussion for the approval of **Rupatadina Trombicor 10 mg tablets**. The procedure was finalised on Octubre 2016. For information on changes after this date please refer to the module 'Update'.

INTRODUCTION

This decentralised application concerns a generic version of Rupatadine fumarate. In this Assessment Report, the name Rupatadine is used.

The originator product is Rupafin® 10 mg tablets by J. Uriach y Compañía, S.A., Spain was granted on July 04th, 2001 in Spain.

This marketing authorization application for Rupatadine 10 mg tablets, is submitted under Directive 2001/83/EC Article 10 (1) "generic application" in cross-reference to the non-clinical and clinical data supporting the European marketed formulation of the reference products in Europe, Rupafin® 10 mg tablets, by J. Uriach y Compañía, S.A.

The Concerned Member State involved in this procedure is FR.

Rupatadine is indicated in the symptomatic treatment of allergic rhinitis and urticaria in adults and adolescents (over 12 years of age).
Rupatadine 10 mg tablet is not recommended for use in children below age 12. In children aged 6 to 11 years, the administration of rupatadine 1 mg/ml oral solution is recommended. The recommended dose is 10 mg (one tablet) once a day, with or without food. As there is no clinical experience in patients with impaired kidney or liver functions, the use of Rupafin® 10 mg tablets is at present not recommended in these patients.

A comprehensive description of the product information is given in the SmPC.

RECOMMENDATION

Based on the review of the data on quality, safety and efficacy, the Member States have granted a marketing authorisation for **Rupatadine Trombicor 10 mg tablets** for J. Uriach y Compañía, S. A.

I. SCIENTIFIC OVERVIEW AND DISCUSSION

II-1 Quality aspects

DRUG SUBSTANCE

The ASMF procedure has been used by the Applicant to support the drug substance quality.

The chemical-pharmaceutical documentation and quality overall summary in relation to rupatadine fumarate are of sufficient quality in view of the present European regulatory requirements.

The control tests and specifications for drug substance are adequately drawn up

The reference materials used are well characterised according to the information provided in the Applicant's part of this ASMF. The quality profile of the reference materials used in routine controls is correctly established for the proposed used.

Stability studies have been performed with the drug substance. No significant changes in any parameters were observed. The proposed retest period of 60 months is justified.

The information provided in the restricted part and applicant's part of this ASMF is considered suitable to support the proposed quality of rupatadine fumarate,

DRUG PRODUCT

Description of the product

The dosage form is a conventional tablet containing 12.8 mg of rupatadine fumarate (equivalent to 10 mg of rupatadine free base).

The qualitative composition of the tablet is as follows:

- Rupatadine fumarate (1)
- Pregelatinized starch
- Mycrocristalline cellulose
- Red Iron oxide E172
- Yellow Iron oxide E172
- Lactose monohydrate
- Magnesium stearate

(1) Equivalent to 10 mg of rupatadine free base.

The packaging consists in a PVC/PVDC/Aluminium blister

Pharmaceutical development

The pharmaceutical development has been properly described. The function of the excipientes has been discussed. The manufacturing process is described in detail.

The validation studies show that the manufacturing process for the product is suitable for routine production of the medicinal product.

Excipients

The information provided is adequate. These excipients are described in European Pharmacopoeia and they are analysed according to the corresponding monographs.
None of the excipients included in this medicinal product are of human or animal origin except lactose and is in accordance with CPMP/CVMP "Note for guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Product" (EMA/410/01, Rev 03)

Product specification

Specifications proposed are adequate. The product specifications cover appropriate parameters for this dosage form. The limits proposed for the different parameters have been adequately justified.

All analytical methods have been correctly validated following the ICH Q2 (R1) Guideline.

Container closure system

The proposed packaging material PVC/PVDC/Aluminium blister is suitable for the required dosage form and that used in the stability studies, the information provided is satisfactory

Stability

The following shelf life/storage conditions for Rupatadine Biohorm 10 mg Tablets are accepted: 3 years (supported by the results presented) in PVC/PVDC/Aluminium blister without any special condition of storage. Keep the blisters in the outer carton
The expiration period shelf life for the tablets is calculated according to the NFG on start of shelf life of the finished Dosage Form (CPMP/QWP/072/96)

II-2 Non-clinical aspects

A non-clinical overview on the pharmacology, pharmacokinetics and toxicology of the active substance has been provided, which is based on up-to-date and adequate scientific literature.

The submitted application concerns tablets with the active substance in the same form as the reference product.

The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate and the Member States agreed that no further non-clinical studies are required.

Environmental Risk Assessment (ERA)

No Environmental Risk Assessment was submitted. This was justified by the Applicant as the introduction of Rupatadine Trombicor 10 mg tablets manufactured by J. Uriach y Compañía, S.A., is considered unlikely to result in any significant increase in the combined sales volumes for all rupatadine containing products and the exposure of the environment to the active substance. Thus, the ERA is expected to be similar and not increased.

The justification for the absence of ERA is considered acceptable.

II.3 Clinical aspects

Introduction

Rupatadine fumarate is well-known drug with established efficacy and safety.

No new clinical efficacy or safety studies were conducted, which is acceptable for this abridged application. A clinical overview has been provided, which is based on scientific literature. The Member States agreed that no further clinical studies are required.

For this generic application, the MAH has not submitted a bioequivalence study, which is discussed below.

Biowaiver

This marketing authorization application for Rupatadine 10 mg tablets, is submitted under Directive 2001/83/EC Article 10 (1) ñgeneric applicationò in cross-reference to the non-clinical and clinical data supporting the European marketed formulation of the reference products in Europe, Rupafin® 10 mg tablets, by J. Uriach y Compañía, S.A.
The reference medicinal product is Rupafin® 10 mg tablets (J. Uriach y Compañía, S.A.), which was first approved in the European Union on July 04th, 2001 in Spain by means of a national procedure and mutual recognition procedure was used later to get the marketing authorisation in the rest of European countries.
Regarding the bioequivalence, this application does not need to demonstrate the bioequivalence with the reference product based on the following reasons:

- Rupafin 10 mg tablets (reference) and Rupatadine 10 mg tablets have the identical quantitative and qualitative composition on active substance and excipients and also the same packaging material.
- The manufacturers of the active substance and excipients used in the manufacturing of Rupatadine 10 mg tablets are the same as for the reference product.
- Rupatadine 10 mg tablets is manufactured and controlled by the same manufacturing process and analytical procedures as the reference product.

- The responsible for the manufacturing and batch control of Rupatadine 10 mg tablets is the same as the reference product.

A bioavailability study is therefore not required to demonstrate bioequivalence, and none is provided in this application.

Bioequivalence

Not applicable (see above).

Risk Management Plan

A risk management plan in accordance with the requirements of Directive 2001/83/EC as amended has been submitted.

No additional risk minimization activities were required beyond those included in the product information.

Discussion on the clinical aspects

Based on the statistical analysis submitted by the Applicant the test product is equivalent to the reference product.

Efficacy and safety of the active substances rupatadine is well documented for the reference medicinal product. The design of the submitted bioequivalence study is adequate and the results allow us to conclude bioequivalence with the reference.

III OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The application contains an adequate review of published clinical data.

The SmPC, PIL and labelling are considered satisfactory and consistent with the information for the reference medicinal product. The user testing of the Package Information Leaflet has been tested in accordance with Article 59(3) of Directive 2001/83/EC, as amended by Directive 2004/27/EC.

The benefit/risk balance was considered to be positive.

Agreement between Member States was reached during the procedure. The decentralised procedure was finalised with a positive outcome in October 2016.