LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Ebastine Sandoz
(ebastine)

SE/H/1209/01-02/DC

This module reflects the scientific discussion for the approval of Ebastine Sandoz. The procedure was finalised at 2013-12-19. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Ebastine Sandoz, 10 mg and 20 mg, orodispersible tablet, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Sandoz A/S, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and Belgium, Spain and Italy as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Ebastel, 10 mg, film-coated tablet, authorised in Spain since 1989, with Laboratorios Almirall, S.A., as marketing authorisation holder.
The reference product used in the bioequivalence study is Ebastel Forte Flas, 20 mg, orodispersible tablet, from Spain with Laboratorios Almirall, S.A, as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Ebastine Sandoz is presented in the form of orodispersible tablets/ containing 10 mg or 20 mg of ebastine. The excipients are aspartame, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, peppermint flavour, colloidal anhydrous silica and StarLac (a mixture of maize starch and lactose monohydrate). The tablets are packed in blisters.

II.2 Drug Substance

Ebastine has a monograph in the Ph. Eur.

Ebastine is a white powdery material practically insoluble in water and sparingly soluble in methanol. The structure of ebastine has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism is presented. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The active 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 under ICH conditions have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Ebastine Sandoz, orodispersible tablets are formulated using excipients described in the current Ph Eur, except for peppermint flavour (approved by the FDA) and StarLac (tested against an in-house specification). All raw materials used in the product are of vegetable origin or has demonstrated compliance with Commission Directive 2003/63/EC and the NfG on

Minimising the risk of transmitting Animal Spongiform Encephalopathy Agents via human and veterinary medicinal products (EMEA/410/01).

The product development has taken into consideration the physico-chemical characteristics of the active substance.

The manufacturing process has been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control and ensure both batch to batch reproducibility and compliance with the product specification.

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 under ICH conditions have been performed and data presented to support the shelf life claimed in the SPC, with the storage precaution 'Store in the original package in order to protect from light'.

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 37 healthy volunteers, comparing Ebastine, 20 mg, orodispersible tablet with Ebastel Forte Flas, 20 mg, orodispersible tablet under fasting conditions. The study was conducted at Algorithme Pharma Inc, Quebec, Canada between 10th July and 25th August 2009. Blood samples were collected pre-dose and up to 96 hours post-dose. The study design is considered acceptable. Plasma concentrations of the active metabolite carebastine were determined with an adequately validated LC-MS/MS method. Ebastine is considered as an inactive pro-drug which is eliminated quickly with very low plasma concentrations and it is therefore acceptable to demonstrate bioequivalence based on plasma concentrations of the active metabolite carebastine. For AUC_{0-t} and C_{max} of carebastine the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

Based on the submitted bioequivalence study, Ebastine Sandoz, is considered bioequivalent with Ebastel Forte Flas.

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.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

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 Ebastine Teva SE/H/955/01-02/DC. The bridging report submitted by the applicant has been found acceptable.

The results of the conducted bioequivalence study can be extrapolated to other strengths since the criteria for biowaiver for additional strengths are fulfilled according to the Guideline on the investigation of bioequivalence.

The risk/benefit ratio is considered positive and Ebastine Sandoz, 10 mg and 20 mg, orodispersible tablet, is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Ebastine Sandoz, 10 mg and 20 mg, orodispersible tablet, was successfully finalised on 2013-12-19.

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Public Assessment Report – Update

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)

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