LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Ebastine Teva
(ebastine)

SE/H/955/01-02/DC

This module reflects the scientific discussion for the approval of Ebastine Teva . The procedure was finalised at 2011-02-21. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Teva Sweden AB has applied for a marketing authorisation for Ebastine Teva 10 and 20 mg orodispersible tablets claiming essential similarity to Ebastel 20 mg oral lyophilisate marketed in Spain by Laboratorios Almirall, S.A. The product contains ebastine as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Ebastel Forte Flas oral lyophilisates marked by Laboratorios Almirall, S.A in Spain.

II. QUALITY ASPECTS

II.1 Introduction

Ebastine Teva 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 Teva, orodispersible tablets is 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 support the shelf life claimed in the SPC, with the storage precautions '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 40 healthy volunteers, comparing Ebastine Teva, 20 mg, orodispersible tablets with Ebastel Forte Flas, 20 mg, oral lyophilisate, under fasting conditions without intake of water. 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 carebastine were determined with an adequately validated LC/MS/MS method. For carebastine 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%.

Evaluation of bioequivalence was based on the active metabolite carebastine. Taken into account data on exposure, protein binding and *in vitro* activity the contribution to the overall pharmacological activity will be about 1000-fold higher for carebastine compared to ebastine. In accordance with the document *EMEA/618604/2008 Rev. 1* the bioequivalence evaluation could therefore be based on the metabolite carebastine.

In conclusion: based on the submitted bioequivalence study/, Ebastine Teva 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
The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was English.
The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

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 Note for Guidance on the Investigation of Bioavailability and Bioequivalence.

The risk/benefit ratio is considered positive and Ebastine Teva 10 and 20 mg orodispersible tablets are recommended for approval.

VI. APPROVAL

The Decentralised procedure Ebastine Teva 10 and 20 mg orodispersible tablets was successfully finalised on 2011-02-21.

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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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