LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Telomens
(Rivastigmine tartrate)

SE/H/903/01-04/DC

This module reflects the scientific discussion for the approval of Telomens. The procedure was finalised at 2010-12-08. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

ELPEN Pharmaceutical Co. Inc (SA) has applied for a marketing authorisation for Telomens, hard capsules, 1,5 mg, 3 mg, 4,5 mg and 6 mg claiming essential similarity to Exelon 1,5 mg, hard capsules marketed the EU by Novartis Europharm Limited (UK). The product contains rivastigmine tartrate as active substance. For approved indications see the Summary of Product Characteristics. The reference products used in the bio-equivalence study are Exelon, 3 mg, hard capsules and Exelon 6 mg hard capsules from United Kingdom.

II. QUALITY ASPECTS

II.1 Introduction

Telomens is presented in the form of hard capsules containing rivastigmine tartrate 2.4, 4.8, 7.2 and 9.6 mg, corresponding to 1.5, 3, 4.5 and 6 mg respectively of rivastigmine. The excipients are microcrystalline cellulose, colloidal anhydrous silica, hypromellose, magnesium stearate, gelatine, titanium dioxide, red iron oxide, sunset yellow and quinoline yellow. The capsules are packed in PVC-Alu blisters.

II.2 Drug Substance

Rivastigmine tartrate does not have a monograph in the Ph Eur.

Rivastigmine tartrate is a white or almost white, crystalline powder which is very soluble in water, methanol and methylene chloride, and freely soluble in ethanol. The structure of rivastigmine tartrate has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on solubility, dissolution, polymorphism and chirality 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/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

Telomens, hard capsules are formulated using excipients described in the current Ph Eur, except for the hard capsules which are controlled according to acceptable in house specifications. All raw materials used in the product are of vegetable origin except for gelatine for which is 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; 18 months when stored below 30 °C.

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

The submitted bioequivalence studies for the 3 mg and 6 mg formulations were randomised, two-treatment, two-period, two-sequence single-dose crossover studies conducted in 47 respectively 48 healthy volunteers under fed conditions. For the 6 mg study pre-medication with 1 mg of Kytril inj/inf (granisetron hydrochloride) intravenously was done 15 minutes before administration of investigational drug, to increase tolerability of the drug and decrease adverse events like nausea and/or vomiting. The submitted studies demonstrated bioequivalence between Telomens 3 mg and 6 mg capsules are Exelon 3 mg and 6 mg capsules respectively.

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 Telomens, hard capsules, 1,5 mg, 3 mg, 4,5 mg and 6 mg is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Telomens, hard capsules, 1,5 mg, 3 mg, 4,5 mg and 6 mg was successfully finalised on 2010-12-08.

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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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