LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Risedronate Bluefish
Risedronate sodium

SE/H/934/01/DC

This module reflects the scientific discussion for the approval of Risedronate Bluefish. The procedure was finalised at 2010-11-30. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se

I. INTRODUCTION

Bluefish Pharmaceutical AB has applied for a marketing authorisation for “Risedronate Bluefish 35 mg tablets claiming essential similarity to Fortipan 30 mg film coated tablets marketed in Sweden by Procter & Gamble Pharmaceuticals UK Ltd. The product contains risedronate as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is “Actonel, 35 mg film coated tablets marketed by Procter & Gamble Pharmaceuticals in UK.

II. QUALITY ASPECTS

II.1 Introduction

Risedronate Bluefish is presented in the form of tablets containing 40.2 mg risedronate sodium hemipentahydrate which corresponds to 35mg risedronate sodium. The excipients starch pregelatinised, microcrystalline cellulose, crospovidone and magnesium stearate are controlled according to respective monographs in Ph.Eur. The tablets are coated with the coating agent Opadry white II OY-LS-28908 consisting of titanium dioxide, lactose monohydrate, Macrogol/PEG 4000 and hypromellose. The tablets are packed in PVC/PE/PVDC/Aluminium blisters.

II.2 Drug Substance

Risedronate sodium hemipentahydrate does not have a monograph in the Ph Eur.

Risedronate sodium hemipentahydrate is a white or almost white fine-crystalline powder which is soluble in water and in diluted solutions of alkali, practically insoluble in methanol and methylene chloride. The structure of risedronate sodium hemipentahydrate 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/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

Risedronate Bluefish 35 mg film coated tablets is formulated using excipients described in the current Ph Eur. All raw materials used in the product are of vegetable origin except for lactose monohydrate for which 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) has been demonstrated.

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 no special storage precautions.

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

In support of the application, one single center, randomised, single dose, laboratory-blinded, 2-period, 2-sequence, crossover design in 109 healthy male and female subjects (100 completed) with Risedronate 35 mg film-coated tablets under fasting conditions was submitted. Plasma concentrations of risedronate were determined with a validated HPLC/MS/MS method. The 90% CI for AUC_{0-t} and C_{max} were within the conventional acceptance range of 80-125%. Bioequivalence has been sufficiently demonstrated.

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 testing of the package leaflet has not been performed, but an acceptable bridging to a test for a similar product has been made.

The applicant has performed a bridging to the user test of the Risedronate 35mg film-coated tablet, MAH: Pharmanten S.A. Greece.
This leaflet was assessed and accepted in DK/H/1277/001/DC, DK/H/1335/001/DC and DK/H/1468/001-002/DC.

The risk/benefit ratio is considered positive and Risedronate 35mg film-coated tablet is recommended for approval.

VI. APPROVAL

The Mutual recognition/Decentralised procedure for Risedronate Bluefish 35 mg tablets was successfully finalised on 2010-11-30.

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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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