LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Pramipexol Bluefish, 0.18 mg, 0.35 mg, 0.7 mg, tablet
(Pramipexole dihydrochloride monohydrate)

SE/H/785/01-03/DC

This module reflects the scientific discussion for the approval of Pramipexol Bluefish. The procedure was finalised at 2009-12-21. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Bluefish has applied for a marketing authorisation for Pramipexol Bluefish, tablet, 0,18 mg, 0,35 mg, 0,70 mg , claiming essential similarity to Mirapexin, tablet, 0,18 mg, 0,35 mg, 0,70 mg (of reference product)" marketed in Sweden/ the EU by Boering Ingelsheim. The product contains pramipexol as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Mirapexin, tablet marketed by Boering Ingelsheim in Spain.

II. QUALITY ASPECTS

II.1 Introduction

Pramipexol Bluefish is presented in the form of tablets containing 0,18 mg, 0,35 mg, 0,70 mg of pramipexol which corresponds to 0,25 mg, 0,50 mg, and 1,0 mg of pramipexole dihydrochloride monohydrate. The excipients are maize starch, mannitol, povidone, colloidal anhydrous silica and magnesium stearate.

The tablets are packed in aluminium blister.

II.2 Drug Substance

Pramipexol does not have a monograph in the Ph Eur. A draft monograph has recently been published in pharmeuropa.

Pramipexol is a white, crystalline powder which is freely soluble in water, independent of pH. The structure of Pramipexol has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism, chirality, Pka and values 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

Pramipexol Bluefish is formulated using excipients described in the current Ph Eur. All raw materials used in the product are of vegetable origin/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.

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

To support the application, the applicant submitted one single dose bioequivalence study comparing Pramipexole Bluefish 0.18 mg tablets with Mirapexin 0.18 mg tablets. The application concerns three strengths; 0.18 mg, 0.35 mg and 0.7 mg and a bioequivalence study has been performed with the lowest strength, i.e. the 0.18 mg tablet. A biowaiver for the 0.35 mg and 0.7 mg is acceptable since the criteria according to the Note for Guidance on the Investigation of Bioavailability and Bioequivalence CPMP/EWP/QWP/1401/98, section 5.4, are fulfilled, e.g. linear pharmacokinetics for pramipexole has been demonstrated. The study had a single center, open-label, laboratory-blinded, randomized, single dose, two-period, crossover design and was conducted by Quinta-Analytica, Czech Republic, in 2008. The study site has been inspected by European authorities and found to be GCP compliant. The study design was deemed adequate. Bioequivalence between the test and the reference formulations was demonstrated for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max} of pramipexole.

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 been performed and is acceptable.

The risk/benefit ratio is considered positive and Pramipexol Bluefish, tablet, 0,18 mg, 0,35 mg, 0,70 mg is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Pramipexol Bluefish, tablet, 0,18 mg, 0,35 mg, 0,70 mg was successfully finalised on 2009-12-21.

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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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