IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Levofloxacin Bluefish 500 mg film-coated tablets
Levofloxacin
PA1436/019/002

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

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I. INTRODUCTION

This product was initially authorised under procedure number SE/H/0889/001-002/DC with the SE as RMS. The responsibility of RMS was transferred to Ireland on 07/10/2020 under procedure number [iIE/H/1152/001-002/DC.
Please note the following detail for the product in IE:
Marketing Authorisation Number: PA1436/019/001-002
Marketing Authorisation Holder: Bluefish Pharma

The current Summary of Product Characteristics (SmPC) for this medicinal product is available on the HPRA website at www.hpra.ie.

The SE public assessment report published at the time of the initial marketing authorisation is provided herein.

I. INTRODUCTION

Bluefish Pharmaceuticals has applied for a marketing authorisation for Levofloxacin Bluefish, film-coated tablet, 250 mg and 500 mg claiming essential similarity to Tavanic, film-coated tablet, 250 mg and 500 mg marketed in Sweden by Sanofi-Aventis AB. The product contains levofloxacin hemihydrate as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bioequivalence study is Tavanic, 500 mg, film-coated tablet from Germany.

II. QUALITY ASPECTS

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II.1 Introduction

Levofloxacin Bluefish is presented in the form of film-coated tablets containing 256 mg or 512 mg of levofloxacin hemihydrate, which corresponds to 250 mg or 500 mg of the levofloxacin. The excipients are microcrystalline cellulose, crospovidone, hypromellose, macrogol, magnesium stearate, povidone, colloidal anhydrous silica, talc, red iron oxide, yellow iron oxide and titanium dioxide. The film-coated tablets are packed in blisters.

II.2 Drug Substance

Levofloxacin hemihydrate does not have a monograph in the Ph Eur.

Levofloxacin hemihydrate is a light yellowish, odourless powder which is sparingly soluble in methanol. The structure of levofloxacin hemihydrate has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on hydrate forms 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

Levofloxacin Bluefish, film-coated tablets are formulated using excipients described in the current Ph Eur, except for the iron oxides which are controlled according to USP. All raw materials used in the product 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, such as poor aqueous solubility and different hydrate forms.

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

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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

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IV.1 Pharmacokinetics

A bioequivalence study comparing the pharmacokinetic profile of Levofloxacin Bluefish 500 mg tablets with Tavanic 500 mg tablets was performed.

The study was an open label, balanced, randomised, two-treatment, two-period, two-sequence, single dose, crossover, comparative oral bioavailability study in 30 healthy, adult, human male subjects under fasting conditions. Levofloxacin in plasma was determined with a validated HPLC-UV method. Bioequivalence was demonstrated for C_{max} and AUC, using conventional acceptance limits of 80-125%.

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 CONCLUSIONS

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

User testing of the package leaflet has been performed and is 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 Note for Guidance on the Investigation of Bioavailability and Bioequivalence.

The applicant has committed to update the product information in accordance with the outcome of the ongoing Article 30 referral of the reference product Tavanic.

VI. REVISION DATE

VII. UPDATES

This section reflects the significant changes following finalisation of the initial procedure.

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
RMS transfer	From SE/H/0889/001-002/DC to IE/H/1152/001-002/DC			