LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Bivalirudin Reig Jofre
(bivalirudin)

SE/H/1499/01/DC

This module reflects the scientific discussion for the approval of Bivalirudin Reig Jofre. The procedure was finalised on 2015-11-19. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Bivalirudin Reig Jofre, 250 mg, powder for concentrate for solution for injection or infusion, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Laboratorio Reig Jofre, S.A, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK, ES, FI, IS, NO and UK as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Angiox, 250 mg, powder for concentrate for solution for injection or infusion, authorised in the Community since 2004, with The Medicines Company UK Ltd as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug 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 confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

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 have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

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

No bioequivalence studies have been conducted. The applied product is to be administered as an aqueous intravenous solution containing the same active substance as the currently authorised product. None of the excipients are known to interact with the drug substance. For this type of product, no bioequivalence studies are required according to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1).

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.

IV.3 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Bivalirudin Reig Jofre.

The “Summary of safety concerns” has been updated following request from the RMS, and is now as follows:

Important identified risks	1. Hypersensitivity including anaphylactic reaction and shock 2. Thrombosis, in particular acute sent thrombosis in patients with STEMI undergoing primary PCI. 3. Brachytherapy 4. Cardiac disorders (Myocardial infarction; Cardiac tamponade; Angina pectoris; Ventricular tachycardia) 5. Haemorrhage 6. Injection site reactions 7. Use in patients with renal or hepatic impairment 8. Medication errors (including reports describing patients receiving bivalirudin bolus without subsequent infusion).
Important potential risk	1.Interaction with other medicinal products

	according to the mechanism of action of Bivalirudin
Missing information	1. Use during pregnancy and breast-feeding 2. Use of bivalirudin in paediatric patients. 3. Effects on ability to drive and use machines

There will be routine pharmacovigilance only. Routine risk minimisation measures include wording in the SmPC. As the originator has additional risk minimisation measures in the form of educational material, and it follows that the generic product also should provide this type of material, additional risk minimisation measures have now been included in the updated RMP (submitted as annex 10 and 11).

The RMP is approved.

V. 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.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The benefit/risk ratio is considered positive and Bivalirudin Reig Jofre, 250 mg, powder for concentrate for solution for injection or infusion, is recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83 in case of a positive benefit risk assessment
N/A
List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC
N/A

VII. APPROVAL

The Decentralised procedure for Bivalirudin Reig Jofre, 250 mg, powder for concentrate for solution for injection or infusion, was positively finalised on 2015-11-19.

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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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