LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Ropivakain Sintetica (ropivacaine)

SE/H/1002/01-05/DC

This module reflects the scientific discussion for the approval of Ropivakain Sintetica. The procedure was finalised at 12 May 2011. 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

Sintetica Italia srl has applied for a marketing authorisation for Ropivakain Sintetica, solution for injection, 2 mg/ml, 5 mg/ml, 7,5 mg/ml and 10 mg/ml and solution for infusion, 2 mg/ml claiming essential similarity to Narop, solution for injection, 5 mg/ml, 7,5 mg/ml and 10 mg/ml and solution for injection/infusion, 2 mg/ml marketed in Sweden by AstraZeneca AB. The product contains ropivacaine as active substance. For approved indications see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

The finished product is presented in the form of a solution for injection containing 2 mg/ml, 5 mg/ml, 7,5 mg/ml and 10 mg /ml of ropivacaine hydrochloride as ropivacaine hydrochloride monohydrate, respectively, and a solution for infusion containing 2 mg/ml ropivacaine hydrochloride as ropivacaine hydrochloride monohydrate.

The excipients are sodium chloride and water for injections. The injections products are filled in 10 ml and 20 ml polypropylene ampoules (with the exception of 5mg/ml that is only 10ml ampoule). The infusion product is filled in 100 ml, 200 ml and 250 ml polypropylene infusion bags.

II.2 Drug Substance

The drug substance ropivacaine hydrochloride monohydrate has a monograph in the Ph Eur.
The drug substance is a white or almost white, crystalline powder soluble in water and in ethanol (96 %) and slightly soluble in methylene chloride. The manufacturer of the drug substance holds a Certificate of Suitability granted by European Directorate for the Quality of Medicines (EDQM). The certificate verifies that the substance is suitably controlled by the current edition of the Ph. Eur. The re-test period stated on the CEP is 36 months.

II.3 Medicinal Product

Ropivakain Sintetica solution for injection or infusion is a sterile, clear, colourless solution for parenteral administration.

The product composition is adequately described.

The development of the product has been satisfactorily performed and explained regarding the choice and functions of excipients. The product contains excipients commonly used in the production of parenteral preparations. No incompatibilities between active and excipients are observed. Excipients are those safe for use for parenteral products.
No preservatives are used in the formulation. None of the material used in the manufacture of the product has human or animal origin.
The packaging materials are standard and shown suitable by the presented stability studies.
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.

Satisfactory physical, chemical and microbiological stability has been demonstrated in stability studies of the product. The data presented support the shelf life claimed in the SPC with the precaution “Do not freeze”.
Chemical and physical in-use stability has been demonstrated for 24 hours at 2-8° C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2–8° 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

Bioequivalence studies have not been included for this application, as it concerns a solution for injection or infusion. Ropivacaine Sintetica is an aqueous solution for parenteral administration and it has the same qualitative and quantitative composition as the reference product Narop. Hence, a bioequivalence study is not needed.

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.

However, the following three areas were not authorised in one or more of the CMSs for the substance ropivacaine.

- Intrathecal use for ropivacaine 5 mg/ml.
- Intra-articular injection in adults for ropivacaine 7.5 mg/ml.
- Peripheral nerve blockage in children from 1 to 12 years for ropivacaine 5 mg/ml.

The data from which these indications were approved in the RMS have been circulated to all CMSs during the procedure. The MAH withdrew the indications intra-articular injection and nerve blockage in children. The indication intrathecal use for the strength 5 mg/ml was accepted by all CMSs.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

User consultation

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of two bridging reports making reference to Ropivakain Fresenius Kabi, NL/H/1575/001-005/DC regarding wording and Prilotekal (Takipril in Germany), DE/H/1507/001/DC regarding lay-out and design. The bridging reports submitted by the applicant have been found acceptable.

The risk/benefit ratio is considered positive and Ropivakain Sintetica, solution for injection, 2 mg/ml, 5 mg/ml, 7,5 mg/ml and 10 mg/ml and solution for infusion, 2 mg/ml, is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Ropivakain Sintetica, solution for injection, 2 mg/ml, 5 mg/ml, 7,5 mg/ml and 10 mg/ml and solution for infusion, 2 mg/ml, was successfully finalised on 12 May 2011.

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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)

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
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