LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Clariscan
(gadoteric acid)

SE/H/1562/01-02/DC

This module reflects the scientific discussion for the approval of Clariscan. The procedure was finalised on 2017-01-24. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Clariscan, 0,5 mmol/ml, solution for injection and solution for injection in pre-filled syringe, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, GE Healthcare AS, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and AT, DE, DK, ES, FI, FR, IE, IS, IT, 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 Dotarem, 279.3 mg/ml, solution for injection authorised in Sweden since 1995, with Guerbet as marketing authorisation holder.

For CMS: AT, DK, FI and IS the concept of European Reference Product (ERP) is used with reference to the reference product authorised in the RMS, Dotarem, 279,3 mg/ml, solution for injection.

For approved indications, see the Summary of Product Characteristics.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83 and conditions to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

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 study has been submitted. 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 (RMP) 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 Clariscan.

Following comments from RMS and CMS during the procedure, version 2.0 of the RMP (dated 23 August 2016) was approved with the following list of safety concerns:

Summary table of safety concerns in RMP version 2.0

Important identified risks	Hypersensitivity including anaphylaxis Nephrogenic systemic fibrosis Convulsions
Important potential risks	Gadolinium accumulation in organs and tissues other than brain tissues Accumulation and retention of gadolinium in the brain
Missing information	Clinical significance of Gadolinium accumulation in organs and tissues other than brain tissues Clinical significance of gadolinium retention in the brain Use in pregnancy

Pharmacovigilance Plan
Routine pharmacovigilance and no additional pharmacovigilance activities were proposed by the applicant, which was endorsed.

Risk minimisation measures
Routine risk minimisation and no additional risk minimisation activities were proposed by the applicant, which was endorsed.

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 quality of the generic product, Clariscan, is found adequate. There are no objections to approval of Clariscan, from a non-clinical and clinical point of view. The product information is acceptable.
The application is therefore recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83 in case of a positive benefit risk assessment

Post approval commitments
The applicant has committed to adopt the Core summary of product characteristics (SmPC) and package leaflet for gadoteric acid. A variation application will be submitted after final publication of the Core SmPC in 2017.

List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

The Decentralised procedure for Clariscan, 0,5 mmol/ml, solution for injection and solution for injection in pre-filled syringe was positively finalised on 2017-01-24.

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Public Assessment Report – Update

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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