COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Dexmedetomidine Seacross 100 microgram/ml concentrate for solution for infusion (dexmedetomidine hydrochloride)

NL/H/5281/001/DC

Date: 2 March 2026

This module reflects the scientific discussion for the approval of Dexmedetomidine Seacross 100 microgram/ml concentrate for solution for infusion. The procedure was finalised on 9 July 2024. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Dexmedetomidine Seacross 100 microgram/ml concentrate for solution for infusion, from Seacross Pharma (Europe) Limited.

The product is indicated:

- For sedation of adult Intensive Care Unit (ICU) patients requiring a sedation level not deeper than arousal in response to verbal stimulation (corresponding to Richmond Agitation-Sedation Scale (RASS) 0 to -3).
- For sedation of non-intubated adult patients prior to and/or during diagnostic or surgical procedures requiring sedation, i.e. procedural/awake sedation.

A comprehensive description of the up-to-date indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC, which concerns a generic application.

In this decentralised procedure, essential similarity is proven between the new product and the innovator product Dexdor 100 micrograms/ml concentrate for solution for infusion, which has been registered in the EEA via a centralised procedure (EMEA/H/C/002268) by Orion Corporation since 15 September 2011.

The concerned member states (CMS) involved in this procedure was Germany.

II. QUALITY ASPECTS

II.1 Introduction

Dexmedetomidine Seacross is a concentrate for solution for infusion (sterile concentrate). The concentrate is a clear, colourless solution, pH 5.0 – 6.5 and osmolarity 275 – 295 mOsmol/kg.

Each 1 ml of concentrate contains as active substance dexmedetomidine hydrochloride equivalent to 100 micrograms dexmedetomidine.

Each 2 ml ampoule contains 200 micrograms of dexmedetomidine.

The concentration of the final solution after dilution should be either 4 micrograms/ml or 8 micrograms/ml.

The excipients are: sodium chloride and water for injections.

The concentrate for solution for infusion is packed in 2 ml type I colourless glass ampoules.

II.2 Drug Substance

The active substance is dexmedetomidine hydrochloride (HCl), an established active substance not described in the European (Ph.Eur.) or British (BP) Pharmacopoeia. However, the substance is monographed in the United States Pharmacopoeia (USP). Furthermore, a monograph on the finished product (Dexmedetomidine Injection) is available in the USP. Dexmedetomidine HCl is a white or almost white, hygroscopic, crystalline powder, very soluble in water freely soluble in methylene chloride and DMF, as well as slightly soluble in acetonitrile. Dexmedetomidine HCl exhibits polymorphism. For this product, polymorphic form A is consistently produced.

The Active Substance Master File (ASMF) procedure is used for the active substance. The main objective of the ASMF procedure, commonly known as the European Drug Master File (EDMF) procedure, is to allow valuable confidential intellectual property or 'know-how' of the manufacturer of the active substance (ASM) to be protected, while at the same time allowing the applicant or marketing authorisation holder (MAH) to take full responsibility for the medicinal product, the quality and quality control of the active substance. Competent Authorities/EMA thus have access to the complete information that is necessary to evaluate the suitability of the use of the active substance in the medicinal product.

Manufacturing process

The manufacturing process consists of two chemical stages, followed by diastereomeric resolution and salt-forming stages, as well as a final purification stage. Adequate specifications have been adopted for starting materials, solvents and reagents. The active substance has been adequately characterised and the manufacturing process is described in sufficient detail.

Quality control of drug substance

The active substance specification is considered adequate to control the quality and meets the requirements of the in-house methods for drug substance control by the manufacturer. All in-house methods are adequately described and validated in the dossier. Forced degradation studies demonstrated that the methods for control of related substances and assay are stability indicating. The specification is in-line with the various European guidelines.

Batch analytical data demonstrating compliance with this specification have been provided for three production size batches.

Stability of drug substance

Stability data on the active substance have been provided for three commercial size batches in accordance with applicable European guidelines. Based on the data submitted, a retest period could be granted of 12 months when stored under the stated conditions.

II.3 Medicinal Product

Pharmaceutical development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

The choice of excipients is justified and their functions explained. The choices of the packaging and manufacturing process are justified in relation to the innovator. Pharmaceutical development focused on Critical Quality Attributes (CQAs) and especially how these CQAs were impacted by changes in manufacturing process.

Manufacturing process

The manufacturing process has been validated according to relevant European/ICH guidelines. Data of three exhibit batches have been provided in accordance with the relevant European guidelines.

Control of excipients

The excipients comply with Ph. Eur. requirements were applicable, or with other relevant compendial requirements. These specifications are acceptable.

Microbiological attributes

To support the sterility of the finished drug product, the Sterility test (Ph.Eur. 2.6.1) and the test for Bacterial Endotoxins (Ph.Eur. 2.6.14) are implemented in the drug product specification.
Furthermore, the drug product manufacturing process is well-controlled and includes safeguards to prevent microbial contamination of the finished drug product. Such safeguards include:

- Use of water for injection (including regular monitoring for microbiological quality) for preparation of the bulk solution
- Use of sterilised and depyrogenised primary packaging material (ampoules) in the manufacturing process

Quality control of drug product

The finished product specifications are adequate to control the relevant parameters for the dosage form. The specification includes tests for appearance, identification, clarity and colour of solution, uniformity of dosage units, pH, osmolarity, visible and sub-visible particles, extractable volume, BET, sterility, assay, related substances and enantiomeric purity. Limits in the specification have been justified and are considered appropriate for adequate quality control of the product. An adequate nitrosamines risk evaluation report has been provided. No risk for presence of nitrosamines in the drug product was identified.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data from three commercial size batches from the proposed production site have been provided, demonstrating compliance with the specification.

Stability of drug product

Stability data on the product have been provided from three commercial size batches stored at 25°C/ 60% RH (36 months) and 40°C/75% RH (6 months) in accordance with applicable European guidelines. A photostability study has been performed on the drug product ampoules. The conditions of the study were selected according to ICH Q1B. The drug product did not show any signs of degradation after exposure to light in the primary packaging material. The drug product was hence not considered to be photosensitive. On basis of the

data submitted, a shelf life was granted of 3 years. No specific storage conditions needed to be included in the SmPC or on the label.

In-use stability data have been provided demonstrating that the product remains stable for 24 hours following dilution, when stored at 25°C.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Dexmedetomidine Seacross has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.

No post-approval commitments were made.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

Since Dexmedetomidine Seacross is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment was therefore not deemed necessary.

III.2 Discussion on the non-clinical aspects

This product is a generic formulation of Dexdor which is available on the European market. Reference was made to the preclinical data obtained with the innovator product. A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which was based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. Therefore, the member states agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Introduction

Dexmedetomidine hydrochloride is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The member states agreed that no further clinical studies are required, besides the one biowaiver which is discussed below.

IV.2 Pharmacokinetics

Dexmedetomidine Seacross 100 microgram/ml concentrate for solution for infusion is a parenteral formulation and therefore fulfils the exemption mentioned in the Note for Guidance on bioequivalence "5.1.6 parenteral solutions", which states that a bioequivalence study is not required if the product is administered as an aqueous intravenous solution containing the same active substance in the same concentration as the currently authorised reference medicinal product (NfG CPMP/EWP/QWP 1401/98). The quantitative composition of Dexmedetomidine Seacross is entirely the same as the originator. Therefore, it may be considered as therapeutic equivalent, with the same efficacy/safety profile as known for the active substance of the reference medicinal product. The current product can be used instead of its reference product.

Biowaiver

The generic medicinal product Dexmedetomidine Seacross is equivalent to the reference product of Dexdor, in line with Directive 2001/83/EC, article 10.2 (b):

a. They have the same qualitative and quantitative composition of an active substance,
b. They have the same pharmaceutical form, i.e. concentrate for solution for infusion,
c. They are considered bioequivalent, since it regards aqueous intravenous solutions in which the excipients do not interact with the drug substance or affect the disposition of the drug substance.

A clinical trial is not required for this application, since Dexmedetomidine Seacross is a parenteral solution for intravenous use, and is of the same type (aqueous solution), contains the same concentration of dexmedetomidine hydrochloride and the same excipients as Dexdor.

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 Dexmedetomidine Seacross. At the time of approval, the most recent version of the RMP was version 0.2 dated 30 April 2021.

Table 1. Summary table of safety concerns as approved in RMP

Important identified risks	Atrioventricular block Bradycardia Cardiac arrest Hypotension Hypertension Hyperglycaemia Withdrawal syndrome
Important potential risks	Ischaemic heart disease Cortisol suppression Convulsions Hypothermia Respiratory depression Torsade de pointes/QT prolongation Overdose Off-label use
Missing information	Use in pregnancy

The member states agreed that routine pharmacovigilance activities and routine risk minimisation measures are sufficient for the risks and areas of missing information.

IV.4 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Dexdor. The MAH demonstrated through a biowaiver that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of this reference product. Risk management is adequately addressed. This generic medicinal product can be used instead of the reference product.

V. USER CONSULTATION

The package leaflet (PL) 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 PL was English.

The test consisted of two test rounds with 10 participants each. The questions covered the following areas sufficiently: traceability, comprehensibility and applicability.
The results show that the PL 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

Dexmedetomidine Seacross 100 microgram/ml concentrate for solution for infusion has a proven chemical-pharmaceutical quality and is a generic form of Dexdor 100 micrograms/ml concentrate for solution for infusion. Dexdor is a well-known medicinal product with an established favourable efficacy and safety profile.

Since both the reference and current product are intended for parenteral use, no bioequivalence study is deemed necessary. A biowaiver has been granted.

The Board followed the advice of the assessors.

There was no discussion in the CMD(h). Agreement between member states was reached during a written procedure. The member states, on the basis of the data submitted, considered that essential similarity has been demonstrated for Dexmedetomidine Seacross with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 9 July 2024.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
NL/H/5281/001 /IB/001	Change in the (invented) name of the medicinal product - for Nationally Authorised products.	Yes	10-9-2025	Approved	N.A.
NL/H/5281/001 /IA/002	Introduction of , or changes to, a summary of pharmacovigila nce system for medicinal products for human use - Introduction of a summary of pharmacovigila nce system, changes in QPPV (including contact details) and/or changes in the Pharmacovigila nce System Master File (PSMF) location.	No	28-10-2025	Approved	N.A.