LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Desmopressin Newbury
(desmopressin acetate, desmopressin)

SE/H/2788/001-003

This module reflects the scientific discussion for the approval of Desmopressin Newbury. The Public Assessment Report was written in August 2023 by the previous RMS IS after initial procedure IS/H/0502/001-003/DC and is attached at the end of this document. RMS transfer from IS to SE was completed 01 June 2025. For information on changes after this date please refer to the module 'Update'.

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LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report – Update

Procedure number*	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

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Public Assessment Report

Scientific discussion

IS/H/0502/001-003/DC: Desmopressin Newbury

desmopressin acetate

IS/H/0502/001-003/DC

Date: 01.08.2023

This module reflects the scientific discussion for the approval of Desmopressin Newbury. The procedure was finalised at 20.06.2023. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Desmopressin Newbury sublingual tablets, 60, 120, 240 micrograms from Newbury Pharmaceuticals AB.
The product is indicated for*:*

- Treatment of central diabetes insipidus.
- Treatment of primary nocturnal enuresis in children from 5 years of age with a normal ability to concentrate urine.
- Symptomatic treatment of nocturia in adults aged below 65, associated with nocturnal polyuria, i.e. nocturnal urine production exceeding functional bladder capacity.

A comprehensive description of the indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC.

Desmopressin is a structural analogue of the natural antidiuretic hormone, vasopressin.

It differs from this in that the amino group in cysteine is removed and L arginine is replaced by D arginine. This results in a significantly extended duration of action and a total lack of pressor effect in clinically current dosing.

Compared to the natural hormone, desmopressin is characterized by an increased and prolonged antidiuretic activity, while its vasopressor activity is very reduced. Desmopressin acts as a selective agonist at vasopressin V2 receptors, located primarily on the collecting duct cells of the kidney.
Oral administration of a dose of 0.1 to 0.2 mg of desmopressin tablet (corresponding to 60 and 120 micrograms of oral lyophilisate) causes an antidiuretic effect which lasts approximately 8 hours with significant inter- individual variations.

II. QUALITY ASPECTS

II.1 Introduction

Desmopressin Newbury sublingual tablets are:
60 micrograms sublingual tablet
White or almost white, round, biconvex tablet debossed with ‘I’ on one side and plain on other side, with 6.5 mm diameter and 2 mm thickness.

120 micrograms sublingual tablet
White or almost white, octagonal, biconvex tablet debossed with ‘II’ on one side and plain on other side, with 6.5 mm length/ width and 2 mm thickness.

240 micrograms sublingual tablet
White or almost white, square, biconvex tablet debossed with 'III' on one side and plain on other side with 6 mm length/ width and 2 mm thickness.

Carton box containing OPA/Al/PVC/PE-AL standard blisters or unit dose blisters with integrated desiccant layer with 10 tablets each, or HDPE bottle with PP caps.

Drug composition:
Desmopressin acetate

Excipients:
Lactose monohydrate
Maize starch
Citric acid (E 330)
Croscarmellose sodium (E 468)
Magnesium stearate (E 470b)

The excipients and container closure systems are common for this type of dosage form.

II.2 Drug Substance

Desmopressin acetate is a white or almost white fluffy powder, soluble in water, ethanol and glacial acetic acid. It does not show polymorphism.
It is monographed in the European Pharmacopoeia (07:2009:0712).

Stability studies have been conducted and the data provided is sufficient to support the proposed retest period.

II.3 Medicinal Product

Pharmaceutical development

The drug product Desmopressin sublingual tablets was developed as a generic equivalent to Minirin Melt by Ferring from the European market. The product is intended as an immediate release product with a comparable dissolution profile to the reference and acceptable pharmaceutical stability.

Manufacturing process

Due to the low drug load (below 2%), the drug product is regarded as non-standard dosage form. The in-process controls are sufficient for immediate release tablets. The manufacturing process has been described in sufficient detail.

The manufacturing process was validated with three batches. The batch used in the bioequivalence study is part of the performed process validation. A summary of the in-

process information during manufacture is provided to confirm that the proposed Desmopressin sublingual tablets can be manufactured according to the proposals in the dossier. All parameters and attributes were found to be within acceptable ranges and according to acceptance criteria.

Product specification
The proposed drug product specification is acceptable.
Analytical methods were adequately described and validated.
Batch analysis data showing compliance with the proposed release specification were provided.
No risk for the presence of nitrosamine impurities in the drug product was identified.

Stability of drug product
Proposed 30 months shelf-life with special storage conditions with respect to protection from moisture for the finished product in Al/Al blisters and HDPE containers is acceptable.

The pharmaceutical quality of Desmopressin Newbury has been adequately shown.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Information on development, manufacture and control of active substance and medicinal product has been presented in a satisfactory manner. The results of tests carried out indicate satisfactory consistency and uniformity of important product quality characteristics.

III. NON-CLINICAL ASPECTS

III.1 Introduction

Abridged applications avoid the need for repetitive tests on animals and humans.

III.2 Pharmacology, Pharmacokinetics and Toxicology

Pharmacodynamic, pharmacokinetic and toxicological properties of desmopressin are well known. As desmopressin is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. Overview based on literature review is, thus, appropriate.

The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate.

III.3 Ecotoxicity/environmental risk assessment (ERA)

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

IV. CLINICAL ASPECTS

IV.1 Introduction

To support the marketing authorisation application the applicant has conducted one bioequivalence study comparing Desmopressin Newbury (Desmopressin) with the reference product Minirin Melt.
A biowaiver is requested for the lower 60 micrograms and 120 micrograms strengths. This is acceptable as all conditions as stated in the BE Guideline are fulfilled.

IV.2 Pharmacokinetics

Bioequivalence studies
To support the application, the applicant has submitted as report one bioequivalence study.

Statement of GCP compliance is provided. A statement is provided to confirm that the bioequivalence study carried out outside the European Union meets the ethical requirements of the European Union Directive 2001/20/EC.

Study was a randomised, two-treatment, four-period, two-sequence single-dose full replicate crossover study comparing Desmopressin, 240 micrograms, sublingual tablets with Minirin Melt, 240 micrograms, oral lyophilisate under fasting conditions.

The results from the pharmacokinetic and statistical analysis are presented in Table 1 below.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} median, range) for desmopressin.

Treatment	AUC_{0-t} pg*h/ml	C_{max} pg/ml	t_{max} h
Test	390.42 ± 465.95	91.69 ± 88.59	1.50 (0.75 - 16.00)
Replicate Test	312.51 ± 314.94	75.79 ± 53.76	1.50 (0.75 - 8.00)
Pooled Test	351.87 ± 398.28	83.82 ± 73.50	1.50 (0.75 - 16.00)
Reference	346.30 ± 356.07	83.70 ± 75.67	1.50 (0.25 - 6.00)
Replicate Reference	316.67 ± 244.49	75.74 ± 54.67	1.50 (0.00 - 3.00)
Pooled Reference (AUC_{0-t} n=94, C_{max} n=95)	331.80 ± 305.32	79.76 ± 65.89	1.50 (0.00 - 6.00)
*Ratio (90% CI)	97.50 (88.83-107.02)	101.57 (92.77-111.21)	-

AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours
C_{max} maximum plasma concentration
t_{max} time for maximum plasma concentration

**calculated based on ln-transformed data*

Conclusion on bioequivalence studies:
Based on the submitted bioequivalence study, the Desmopressin, 240 micrograms, sublingual tablets is considered bioequivalent with Minirin Melt, 240 micrograms.
A biowaiver is requested for the lower 60 micrograms and 120 micrograms strengths. This is acceptable as all conditions as stated in the BE Guideline are fulfilled.

IV.3 Pharmacodynamics

No new pharmacodynamic studies were presented and no such studies are required for this application.

IV.4 Clinical efficacy

No new clinical efficacy studies were presented and no such studies are required for this application.

IV.5 Clinical safety

No new clinical safety studies were presented and no such studies are required for this application.

IV.6 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 desmopressin.

Summary table of safety concerns as approved in RMP

Important identified risks	None
Important potential risks	None
Missing information	None

Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

IV.7 Discussion on the clinical aspects

Desmopressin Newbury is a generic to Minirin Melt. Abridged applications avoid the need for repetitive tests on animals and humans apart from a conduction of a bioequivalence study.

The application contains an adequate review of published clinical data and the bioequivalence has been shown between applied product and with Minirin Melt.

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

Based on the review of the data on quality, safety and efficacy, the risk-benefit ratio for the application for Desmopressin Newbury, that is indicated for:

- Treatment of central diabetes insipidus.
- Treatment of primary nocturnal enuresis in children from 5 years of age with a normal ability to concentrate urine.
- Symptomatic treatment of nocturia in adults aged below 65, associated with nocturnal polyuria, i.e. nocturnal urine production exceeding functional bladder capacity,

is considered positive and marketing authorisation is recommended.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC.

There are no specific obligations and follow-up measures.

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