

Public Assessment Report

Scientific discussion

Morphine Unimedic **(morphine hydrochloride)**

SE/H/1657/01/DC

This module reflects the scientific discussion for the approval of Morphine Unimedic. The procedure was finalised on 2018-02-28. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

The application for Morphine Unimedic, 1 mg/ml, solution for injection, is a hybrid application made according to Article 10(3) of Directive 2001/83/EC. The applicant, Unimedic Pharma AB applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and Denmark, Finland and Norway as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Morfin Epidural Meda, 0,4 mg/ml, solution for injection, authorised in Sweden since 1985, with Meda AB as marketing authorisation holder.

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 an aqueous solution intended for epidural use and is qualitatively identical and quantitatively similar to the reference product. The applied product consists of a different concentration (i.e. 1 mg/ml) compared to the reference product Morfin Epidural Meda 0.4 mg/ml, 2 mg/ml and 10 mg/ml. Another volume for injection will also be administrated compared with the reference product.

According to the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev1/Corr), for parenteral solutions that are not intravenously administrated, a bioequivalence study can be waived if the type of solution is the same, the concentration of active substance is the same and the product contains the same excipients in similar amounts (or comparable excipients that do not affect the viscosity). In this case, the concentration differs between the applied product and the reference product. However, the new concentration and volumes administrated are within the approved range of concentrations and volumes administrated for the reference product Morfin Epidural Meda 0.4 mg/ml and 2 mg/ml. The doses suggested are also the same as for the reference product. Thus the absence of a bioequivalence study is found acceptable.

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 Morphine Unimedic.

Safety specification

The applicant has made the following safety concerns which are derived from the Contraindications and Warnings and Precautions sections of the SmPC.

Table 1. Summary of safety concerns

Summary of safety concerns	
Important identified risks	• Respiratory depression • Hepatic Impairment • Drug Interactions • Drug dependancy
Important potential risks	• Use in pregnancy and lactation
Important missing information	• None

Pharmacovigilance Plan

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

Risk minimisation measures

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

Summary of the RMP

The submitted Risk Management Plan, signed 17 Feb 2017 is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference for content to Morfin Abcur 10 mg/ml, solution for injection leaflet assessed and accepted 2013-12-10 in SE/H/1354/01/MR and making reference for layout to Fenylefrin Unimedica 0.1 mg, solution for injection leaflet assessed and accepted 2015-10-21. The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The benefit/risk ratio is considered positive and Morphine Unimedic, 1 mg/ml, solution for injection 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 Morphine Unimedic, 1 mg/ml, solution for injection was positively finalised on 2018-02-28.

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)