LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Nystatin Orifarm
(nystatin)

SE/H/1662/01/DC

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

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I. INTRODUCTION

Orifarm Generics A/S has applied for a marketing authorisation for Nystatin Orifarm Oral suspension, 100 000 IU/ml. The active substance is nystatin. Nystatin is fungistatic or fungicidal depending on the concentration achieved and the susceptibility of the fungus.

For approved indications, see the Summary of Product Characteristics.

The marketing authorisation has been granted pursuant to Article 10(3) of Directive 2001/83/EC.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83/EC 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

Pharmacodynamic, pharmacokinetic and toxicological properties of nystatin are well known. As nystatin is a widely used, well-known active substance, no further non-clinical studies are required and the applicant provides none.

III.1 Ecotoxicity/environmental risk assessment

Since Nystatin Orifarm 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

For this type of product the demonstration of therapeutic equivalence can mainly rely on quality data.

IV.2 Pharmacokinetics

For an abridged application for a locally acting, locally applied product, therapeutic equivalence with regard to efficacy and safety should be demonstrated. According to the Note for guidance on the clinical requirements for locally applied, locally acting products containing known constitutes (CPMP/EWP/239/95), pharmacodynamic studies, local availability studies, animal or in vitro data can be considered, depending on situation. Furthermore, the safety and local tolerance have to be addressed appropriately.

Nystatin is a locally acting drug with negligible oral bioavailability. Both Nystatin Orifarm and the originator Mycostatin are oral suspensions. The composition of the applied product is qualitatively identical and quantitatively similar to the reference product, with the exception that the applied product may also contain sodium hydroxide and hydrochloric acid for pH adjustment which is not included in the reference product. Therapeutic equivalence has been sufficiently demonstrated based on comparative *in vitro* data. Thus, no further clinical data are considered necessary.

IV.3 Pharmacodynamics / Clinical efficacy / Clinical safety

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Therapeutic equivalence has been sufficiently demonstrated based on comparative in vitro data. Thus, no further clinical data are considered necessary.

IV.4 Risk Management Plans

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 Nystatin Orifarm.

The RMP has been updated in accordance with the Assessor's proposal (RMP version 1.1, date of sign off 20 July 2017).

Safety specification

Summary table of safety concerns as approved in RMP

Summary of safety concerns	
Important identified risks	• Hypersensitivity reactions, including anaphylactic reactions • Stevens-Johnson syndrome
Important potential risks	None
Missing information	• Use during pregnancy • Use during lactation

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 MAH has satisfactory responded to the questions raised and updated the RMP accordingly.

Issue is resolved

The RMP is approved

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 to Nystimex SE/H/1366/01/DC. 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 Nystatin Orifarm Oral suspension, 100 000 IU/ml is recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC 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 Nystatin Orifarm Oral suspension, 100 000 IU/ml was positively finalised on 2018-02-28.

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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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