LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

# Public Assessment Report

# Scientific discussion

# Kolestyramin Alternova (colestyramine)

# Asp no 2017-0264

**This module reflects the scientific discussion for the approval of Kolestyramin Alternova. The procedure was finalised on 2018-03-06. For information on changes after this date please refer to the module 'Update'.**

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# I. INTRODUCTION

The application for Kolestyramin Alternova, 4 g, powder for oral suspension, sachet, has been submited as a hybrid application according to Article 10(3) of Directive 2001/83/EC. The applicant, Alternova A/S, applies for a marketing authorisation in Sweden through a National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is QUESTRAN LOC, 4 g, powder for oral suspension, sachet authorised in Sweden since 1989, with BRISTOL-MYERS SQUIBB AB as marketing authorisation holder.

The reference product used in the *in vitro* equivalence study is QUESTRAN LOC, 4 g, Powder for oral suspension, sachet from Sweden with BRISTOL-MYERS SQUIBB AB as marketing authorisation holder.

# 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

Colestyramine site of action is the gastrointestinal (GI) tract, i.e. it is a locally acting gastrointestinal drug. Colestyramine is not absorbed or metabolized in the gastrointestinal tract due to its insolubility in water and its high molecular weight, but it absorbs, and combines with, the bile acids in the intestine to form an insoluble complex that is 100% excreted in the faeces, thus it acts at local level. Because the drug is not absorbed into the systemic circulation, pharmacokinetics information is not available.

Since colestyramine is not absorbed, bioequivalence studies are not applicable. Instead, therapeutic equivalence with the reference product has been demonstrated by in vitro equivalence studies.

## 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 Kolestyramin Alternova.

Safety specification

*Summary table of safety concerns as approved in RMP (version 1.2, with DLP 5 Nov 2017).*

| **Summary of safety concern** | |
|---|---|
| Important identified risks | • None |
| Important potential risks | • None |
| 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.

The Risk management plan version 1.2, with DLP 5 November 2017 is approved.

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

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 Swedish.
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

Kolestyramin Alternova, as other ion-exchange resins, is not absorbed or metabolized in the gastrointestinal tract. Therefore bioequivalence studies are not applicable and instead, therapeutic equivalence with the reference product Questran LOC is demonstrated by in vitro equivalence studies (equilibrium binding and kinetic binding studies).

The quality of the hybrid product, Kolestyramin Alternova, is found adequate. There are no objections to approval of Kolestyramin Alternova, 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**

N/A

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

N/A

# VII. APPROVAL

Kolestyramin Alternova, 4 g, powder for oral suspension, sachet was approved in the national procedure on 2018-03-06.

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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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