LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Halzin Mint
Halzin Honung & Citron
Halzin Jordgubb
(amylmetacresol, dichlorobenzyl alcohol)

Asp no: 2014-1585, 2014-1586, 2015-0087

This module reflects the scientific discussion for the approval of Halzin Mint, Halzin Honung & Citron, Halzin Jordgubb. The procedure was finalised on 2016-01-21. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Halzin Mint, Halzin Honung & Citron and Halzin Jordgubb, 0,60 mg/1,20 mg, lozenges, is a hybrid application made according to Article 10(3) of Directive 2001/83/EC. The applicant, Apofri AB, 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 Strepsils, 0,6 mg/1,2 mg, lozenges, authorised in Sweden since 1961, with Reckitt Benckiser Healthcare S.A 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

In order to evaluate the similarity between Halzin lozenges and a reference formulation, a bioavailability study with two formulations containing Amylmetacresol/Dichlorobenzyl alcohol in healthy volunteers was conducted. The study evaluated the similarity in buccal release between the test and the reference formulation.

Study CFA-068 was a randomised, two-treatment, two-period, two-sequence crossover study conducted in 44 healthy volunteers under fasting conditions. Either Test or Reference formulation was administered daily for five consecutive days. The same formulation was administered during the five days within one period, according to the randomization table. On each administration day, the subjects received a lozenge by oropharyngeal route, which remained in the mouth a certain time. After the pre-established time, the volunteer placed it in a container directly from the mouth. The remaining lozenge was then diluted to obtain a matrix in which to measure concentration of amylmetacresol and dichlorobenzyl alcohol. A washout period between administrations of at least 12 hours and a washout between periods at least 7 days was used.

Since the active substances are not absorbed and acts locally a conventional bioequivalence study is not relevant. The method using indirect determination of the release from the tablets by measuring the non-released amounts is considered to be an acceptable approach.

As primary endpoint a comparison of the dissolution profiles of the test formulation compared to the reference by the similarity factor (f2) was performed. The f2 values obtained were above 50, indicating similarity between the test and the reference product.

Conclusion: Therapeutic equivalence has been sufficiently demonstrated.

IV.2 Clinical efficacy and safety

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 data, no further such data have been submitted or are considered necessary.

IV.3 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 Halzin Mint, Halzin Honung & Citron and Halzin Jordgubb.

A RMP version 1.2 has been submitted with data lock point 20 Nov 2014. The summary of safety concerns are listed in the table below.

Summary table of Safety concerns

Summary of safety concerns	
Important identified risk	Hypersensitivity
Important potential risk	None
Missing information	Use in pregnancy

The RMP 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 Portugese.
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

The benefit/risk ratio is considered positive and Halzin Mint, Halzin Honung & Citron and Halzin Jordgubb, 0,60 mg/1,20 mg, lozenges, 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

Halzin Mint, Halzin Honung & Citron and Halzin Jordgubb, 0,60 mg/1,20 mg, lozenges, was approved in the national procedure on 20160121.

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Public Assessment Report – Update

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)

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