LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Treo Hallon
(acetylsalicylic acid/caffeine)

Asp no: 2017-1024

This module reflects the scientific discussion for the approval of Treo Hallon. The procedure was finalised on 2018-05-25. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Meda AB has applied for a marketing authorisation for Treo Hallon, 500/50mg, Effervescent tablet. The active substance acetylsalicylic acid caffeine is the same as in Treo, Effervescent tablet, marketed by Meda AB since 1962-02-01.
No PAR is available for Treo.

For approved indications, see the Summary of Product Characteristics.

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

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 Introduction

The clinical overview based on a review of published literature were submitted to support the product development, clinical pharmacology, efficacy, safety and a conclusion regarding the benefit and risk of the medicinal product.

IV.2 Pharmacokinetics

No new data has been submitted.

The only difference in composition between Treo Hallon and the previously approved products Treo and Treo Citrus is the flavouring agent, and a small difference in mannitol amount to compensate for the difference in weight of the flavour. The flavouring agents are not excipients expected to influence drug pharmacokinetics. Mannitol in higher amounts is known to affect gastrointestinal motility, but in the low amounts present in the Treo effervescent tablets, a risk for an effect on gastrointestinal transit appears low. In addition, the difference in mannitol amount between the different Treo formulations is low, and both acetylic salicylic acid and caffeine are BCSI compounds where formulation effects on pharmacokinetics are not expected.

To conclude, the lack of pharmacokinetic data on Treo Hallon is acceptable, and data from other Treo formulations regarding pharmacokinetics, efficacy and safety are considered valid also for Treo Hallon.

IV.3 Pharmacodynamics, clinical efficacy and safety

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that data from other Treo formulations regarding pharmacokinetics, efficacy and safety are considered valid also for Treo Hallon, additional data is considered not 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 Treo Hallon.

Safety specification

Safety specification are provided in the EU Risk Management Plan for ACETYLSALICYLIC ACID/CAFFEINE, version 2, dated 13-Feb 2018.

Table 3. Summary of safety concerns

Summary of safety concerns	
Important identified risks	• Severe gastrointestinal complications (including ulceration and perforation) • Major haemorrhages including gastrointestinal haemorrhage and intracranial haemorrhage • Severe hypersensitivity including anaphylactic reactions • Maternal, neonatal and foetal toxicity with exposure during the 3rd trimester of pregnancy • Disturbance in renal function homeostasis in patients with renal, hepatic or cardiac insufficiency • Clinically significant drug interactions • Haemolysis in patients with G-6-PD deficiency • Severe skin reactions, including Steven-Johnsons syndrome / Toxic Epidermal Necrolysis.
Important potential risks	• Reye's syndrome
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 updated RMP is accepted.

An updated RMP should be submitted:

- At the request of the MPA;
- 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

No new clinical studies were presented by the applicant. The Applicant has submitted a reasonable amount of the literature data in a clinical overview for Treo products to support this application.

The only difference in composition between Treo Hallon and marketed products Treo/Treo Citrus is the flavouring agent, and a small difference in mannitol amount to compensate for the difference in weight of the flavour. The difference in mannitol amount between the different Treo formulations is low, and both acetylic salicylic acid and caffein are BCSI compounds where formulation effects on pharmacokinetics are not expected. There is no reason to believe that the safety and efficacy profile of Treo Hallon will differ to other Treo products from clinical point of view.

The overall benefit-risk balance of Treo Hallon in the treatment of Headache, toothache, dysmenorrhoea, musculoskeletal pain, fever and migraine is positive.

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

Treo Hallon, 500/50mg, Effervescent tablet was approved in the national procedure on 2018-05-25.

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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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