LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Nitrofurantoin Alternova (nitrofurantoin)

Asp no: 2014-1124

This module reflects the scientific discussion for the approval of Nitrofurantoin Alternova. The procedure was finalised on 2015-07-16. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Nitrofurantoin Alternova, 50 mg, tablet, is a generic application made according to Article 10(1) 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 Furadantin, 50 mg, tablet, authorised in SE since 1958, with Meda AB as marketing authorisation holder.

The reference product used in the bioequivalence study is the same as mentioned above.

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

Nitrofurantoin has a reported oral bioavailability of approximately 90 % according to a study by Hoener and Pattenson (1981). In this study, maximal plasma concentrations following an oral dose occured at approximately 2-3 hours. Antibacterial effect in the urine is obtained within 30 minutes according to the SmPC. Concomitant food intake increases the absorption and decreases the risk for nausea, and the period of active concentration in urine is increased. Therefore nitrofurantoin should be administered with food. The terminal half-life has been reported to be around 30 minutes.

Bioequivalence was evaluated in one single-dose, two-way crossover study conducted in 32 healthy volunteers, comparing nitrofurantoin, 50 mg, tablets (at a dose of 100 mg), with Furadantin, 50 mg, tablets (at a dose of 100 mg), by Meda AB from the Swedish market under fed conditions. The use of the dose of 100 mg was considered sufficiently justified. Blood samples were collected pre-dose and up to 16 hours post-dose. The study design is considered acceptable. Plasma concentrations of nitrofurantoin were determined with an adequately validated LC/MS/MS method. For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%. Thus, bioequivalence has been adequately demonstrated.

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 Nitrofurantoin Alternova.

Summary of Safety Concerns and Planned Risk Minimisation Activities as proposed/ approved in RMP

Summary of safety concerns	
Important identified risks	• Haemolytic anaemia. • Anuria. • Hypersensitivity • Renal insufficiency • Pulmonary reactions • Hepatic disorders
Important potential risks	None.
Missing information	None.

Summary of the RMP

The proposed summary of safety concerns is acknowledged. Generally the RMP should only include safety concerns that are of such severity as to warrant a contraindication or an additional warning, or which affect a significant proportion of the population, adversely affect quality of life or could have serious consequences if left untreated. Thus, the important identified risks are supported.

No ongoing or planned studies in the PhV development plan are proposed. The Applicant comments that this is not applicable as the reference product do not have imposed post-authorisation efficacy studies according to the knowledge of Applicant.

The RMP is considered approvable.

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 Nitrofurantoin 50 mg and 100 mg tablets (the user test was approved by MHRA in the procedure PL 08553/0087-8) . 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 Nitrofurantoin Alternova, 50 mg, tablet, 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

Nitrofurantoin Alternova, 50 mg, tablet, was approved in the national procedure on 2015-07-16.

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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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