LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Nicorette Frukt
(nicotine resinate)

SE/H/1617/03-04/DC

This module reflects the scientific discussion for the approval of Nicorette Frukt. The procedure was finalised on 2017-07-12. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Nicorette Frukt, compressed lozenge, 2 mg and 4 mg, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, McNeil Sweden AB applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and BE, DK, FI, FR, DE, IE, LU, NO, PL as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is NiQuitin, 7 mg/24 hours, transdermal patch authorised in SE since 1994, with Omega Pharma Nordic AB as marketing authorisation holder.

The reference product used in the bioequivalence study is NiQuitin Mint, 2mg, 4 mg, lozenge from SE with Omega Pharma Nordic AB 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

Bioequivalence was evaluated in one single-dose, five-treatment, five-period, eight-sequence crossover study conducted in 104 healthy volunteers who smoke at least 10 cigarettes per day preceding inclusion.

Following a 12-hour nicotine abstinence period, subjects received five out of six investigational products, i.e. Nicorette Pepparmint, 2mg and 4mg lozenge and the two reference products, i.e. Niquitin 2mg and 4mg lozenge and one of two exploratory prototypes (prototypes not relevant for this application). The results from the study with Nicorette Pepparmint can be extrapolated to Nicorette Frukt since the composition is almost identical, only differing in flavour.

The clinical part of the study was conducted between 31 August 2009 and 03 December 2009 at the following two sites: Clinical Pharmacology, McNeil AB in Lund, Sweden and Clinical Trial Unit, Clinical Research and Trial Centre, Lund University Hospital, Lund, Sweden.

On drug administration days, blood-samples were collected pre-dose and up to 12 hours after drug administration. Plasma concentrations of nicotine were determined with a GC-CIMS method. For baseline corrected 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%.

Bioequivalence between Nicorette Frukt 2 mg and 4 mg lozenge and Niquitin 2 mg and 4 mg lozenge has been sufficiently 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 Nicorette Frukt lozenge.

Safety specification

The Applicant has proposed no safety concerns which is accepted in accordance with Var II-13 (SE/H/904/01/II/13) RMP version 5.1 recently approved.

Pharmacovigilance Plan
Routine pharmacovigilance is suitable and no additional pharmacovigilance activities are needed. The RMP is updated accordingly version 5.1

Risk minimisation measures

Routine risk minimisation is suitable and no additional risk minimisation activities are required.

Summary of the RMP

The RMP version 5.1 is approvable.

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

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 Nicorette Pepparmint, 2 mg and 4 mg, compressed lozenges, SE/H/1617/001-002/DC (initially CZ/H/0243/001-002/DC, change of RMS). The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Nicorette Frukt, is found adequate. There are no objections to approval of product name, from a non-clinical and clinical point of view. Bioequivalence between the test and reference product has been adequately demonstrated. 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

The Decentralised procedure for Nicorette Frukt, compressed lozenge, 2 mg and 4 mg was positively finalised on 2017-07-12.

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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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