LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Nicovel Mint
(nicotine)

SE/H/1316/01/DC

This module reflects the scientific discussion for the approval of Nicovel Mint. Please note that the marketing authorisation was first approved with the name "Nicachet" and therefore this name is used throughout the document. The procedure was finalised on 2014-05-23. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Nicachet, 4 mg, oromucosal powder in pouch, is a hybrid application according to Article 10(3) of Directive 2001/83/EC. The applicant, Magle AB, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK, FI and NO as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is originator Nicorette 4 mg medicated chewing gum authorised in SE since 1981, with McNeil Sweden AB as marketing authorisation holder.

The active substance is not considered a new active substance.

II. QUALITY ASPECTS

II.1 Introduction

Nicachet is presented in the form of oromucosal powder in pouch containing 4 mg of nicotine. The excipients are alginic acid, anhydrous sodium carbonate, copovidone, powdered cellulose, peppermint flavour and neohesperidin dihydrochalcone. The pouches are packed in polypropene containers.

II.2 Drug Substance

Nicotine has a monograph in the Ph Eur.

Nicotine is a clear, colourless or brownish viscous liquid which is soluble in water, alcohol and ether. The structure of nicotine has been adequately proven and its physico-chemical properties sufficiently described. The route of synthesis has been adequately described and satisfactory specifications have been provided for the raw materials.

The active substance specification includes relevant tests and the limits for impurities/degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies under ICH conditions have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Niachet oromucosal powder in pouch is formulated using excipients described in the current Ph Eur, except for peppermint flavour which is controlled according to acceptable in house specifications.

The product development has taken into consideration the physico-chemical characteristics of the active substance.

The manufacturing process has been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control and ensure both batch to batch reproducibility and compliance with the product specification.

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 under ICH conditions have been performed and data presented support the shelf life claimed in the SPC, when stored below 30°C in tightly closed container in order to protect from moisture.

III. 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

Nicachet is indicated to facilitate smoking cessation in smokers who are motivated to quit and to facilitate smoking reduction in smokers who are not able or willing to quit smoking.

IV.2 Pharmacokinetics

One bioequivalence study was submitted to support the application. The study was a randomised three-way, single-dose crossover study conducted in 20 healthy volunteers (all smokers ≥7 cigarettes/day for more than 2 years), comparing Nicotine, 4 mg, oromucosal powder in pouch with Nicorette, 4 mg, chewing gum and Nicorette, 1 mg, nasal spray. The study was conducted at Clinical Research and Trial Centre, Skane University hospital, Lund, Sweden between February and March 2011. Blood samples were collected pre-dose and up to 6 hours post-dose. The study design is considered acceptable. Plasma concentrations of nicotine were determined with an adequately validated LC-MS/MS method.

For both AUC_{0-t} corrected for baseline concentrations and uncorrected AUC_{0-t}, the 90% confidence interval for the ratio of the test (Nicotine, 4 mg, oromucosal powder in pouch) and reference (Nicorette, 4 mg, chewing gum) products fell within the conventional acceptance range of 80.00-125.00%. Bioequivalence was not shown with respect to C_{max}, and the C_{max} following Nicotine 4 mg powder in pouch was higher compared to Nicorette 4 mg chewing gum. The point estimate for the uncorrected C_{max} ratio was 127.3% (CI: 108.8-149.0) and the point estimate for the C_{max} ratio corrected for baseline concentrations was 141.0% (CI: 117.2-169.6).

Bioequivalence was shown with respect to AUC but not C_{max} in this study. However, demonstration of bioequivalence is not an absolute requirement in this application and the pharmacokinetic result is considered as supportive to the submitted efficacy/safety studies.

IV.3 Pharmacodynamics

The pharmacodynamics of nicotine is well known. The applicant has provided an adequate clinical overview based on an updated list of literature references up to year 2011 which is considered acceptable.

IV.4 Clinical efficacy

The nicotine efficacy used in the Nicotine Replacement Therapy (NRT) is well documented. The Zonnic pouch, which is a similar product to Nicachet 4 mg oromucosal powder in pouch was effective compared to placebo control and similar to the reference product. Available literature data allows conclude that nicotine provided as an oromucosal powder in pouch has similar effect as nicotine medicated chewing gum. In general, provided results from two clinical studies with Nicachet 4 mg oromucosal powder in pouch suggests that the new product will have similar effect on smoking cessation as the reference product.

IV.5 Clinical safety

The duration of exposure was very limited in the safety and tolerability study (MANS11). The tolerability and safety profile of the NRT is well established and the tolerability of Nicachet 4mg oromucosal powder in pouch was similar to this profile. Given the excipients used in the product, new safety issues besides those already observed for other NRT products are unlikely to occur.

IV.6 Discussion on the clinical aspects

Bioequivalence was shown with respect to AUC but not C_{max} between Nicotine, 4 mg, oromucosal powder in pouch and Nicorette, 4 mg, chewing gum in the presented bioequivalence study. However, demonstration of bioequivalence is not an absolute requirement in this application and the pharmacokinetic result is considered as supportive to the submitted efficacy/safety studies.

Provided efficacy results from two clinical studies with Nicachet 4 mg oromucosal powder in pouch suggests that the new product will have similar effect on smoking cessation as the reference product (Nicorette medicated chewing gum). The overall adverse event profile of the Nicachet 4 mg oromucosal powder in pouch is similar to the already well known profile of similar nicotine replacement products. Based on the available data from presented clinical studies, no signs of significant local safety problems have emerged.

The risk benefit profile for Nicachet 4 mg oromucosal powder in pouch is positive and the product was recommended for approval.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

User consultation

A user consultation with target patient groups on the package information leaflet (PIL) regarding *content* has been performed on the basis of a bridging report making reference to

Zonnic Mint, SE/H/713/01-03/DC. The bridging report submitted by the applicant has been found acceptable.
The *layout* has been evaluated via a user consultation study, focus test, 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 risk/benefit ratio is considered positive and Nicachet, 4 mg, oromucosal powder in pouch, is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Nicachet, 4 mg, oromucosal powder in pouch, was successfully finalised on 2014-05-23.

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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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