

Public Assessment Report

Scientific discussion

Mometasone Phagecon **(mometasone furoate monohydrate)**

Asp no: 2013-0672

This module reflects the scientific discussion for the approval of Mometasone Phagecon. The procedure was finalised at 2014-06-26. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

The application for Mometasone Phagecon, nasal spray, suspension, 50 micrograms/actuation, is a hybrid application made according to Article 10(3) of Directive 2001/83/EC. The applicant, Phagecon, applies through the Swedish National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Nasonex, nasal spray, suspension, 50 micrograms/dose, authorised in France since 1997, with Merck Sharp & Dohme BV as marketing authorisation holder. The reference product used in the bioequivalence study is Nasonex, nasal spray, suspension, 50 micrograms/actuation from UK with Merck Sharp & Dohme Ltd as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Mometasone Phagecon is presented in the form of a nasal spray (suspension) containing 50 micrograms of mometasone furoate (as the monohydrate). The excipients are glycerol, microcrystalline cellulose, carmellose sodium, citric acid monohydrate, polysorbate, benzalkonium chloride, sodium citrate dihydrate and water. The nasal spray is packed in a bottle with a metered dose manual spray actuator.

II.2 Drug Substance

Mometasone furoate is a known active substance and is the subject of a Ph Eur monograph; however the drug product contains mometasone furoate monohydrate for which there is no published compendial monograph.

Mometasone furoate monohydrate is a *white to off white powder* which is *practically insoluble in water and* soluble in acetone. The structure of mometasone furoate monohydrate has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism and chirality is presented. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

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 have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Mometasone Phagecon nasal spray, suspension is formulated using excipients described in the current Ph Eur.

The product development has taken into consideration the physico-chemical characteristics of the active substance, such as poor aqueous solubility and polymorphism.

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 have been performed and data presented support the shelf life claimed in the SPC.

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

Mometasone furoate, administered as an aqueous nasal spray, has a very low systemic bioavailability. Thus, there are very limited pharmacokinetic data for this dosage form. Mometasone furoate nasal spray, suspension is very poorly absorbed from the gastrointestinal tract, and the small amount that may be swallowed and absorbed undergoes extensive first-pass hepatic metabolism prior to excretion in urine and bile.

In addition to comparative *in vitro* data, the applicant has submitted two bioequivalence studies: one with and one without active charcoal blockade. In the study without active charcoal blockade total systemic exposure is evaluated which reflects systemic safety. In the study with charcoal blockade only the fraction of mometasone absorbed through the nasal mucosa will be measured, which could be seen as a surrogate for efficacy. Two pilot studies to determine an appropriate sample size for the pivotal PK studies were also conducted.

Bioequivalence study without active charcoal blockade

Similarity in total systemic exposure was evaluated in one single-dose, two-way crossover bioequivalence study conducted in 48 healthy volunteers, comparing Mometasone furoate 50 µg/actuation nasal spray, suspension by Cipla with Nasonex, 50 µg/actuation nasal spray, suspension under fasting conditions. The study was conducted between 23rd May and 5th July 2011. Blood samples were collected pre-dose and up to 72 hours post-dose. The study design

is considered acceptable. Plasma concentrations of mometasone 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%.

Bioequivalence study with active charcoal blockade

Similarity in efficacy was evaluated in one single-dose, two-way crossover bioequivalence study conducted in 54 healthy volunteers, comparing Mometasone furoate 50 µg/actuation nasal spray, suspension by Cipla with Nasonex, 50 µg/actuation nasal spray, suspension under fasting conditions. The study was conducted between 13th June and 7th July 2011. Blood samples were collected pre-dose and up to 36 hours post-dose. The study design is considered acceptable. Plasma concentrations of mometasone 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%.

Pharmacokinetic conclusion

Bioequivalence was demonstrated both with and without active charcoal blockade which will reflect similarity with respect to both safety and efficacy.

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.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

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 Mometasone Furoate 50 mg/actuations nasal spray, suspension UK/H/5169/001/DC. The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and Mometasone Phagecon, nasal spray, suspension, 50 micrograms/actuation is recommended for approval.

VI. APPROVAL

Mometasone Phagecon, nasal spray, suspension, 50 micrograms/actuation was approved in the national procedure on 2014-06-26.

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)