LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Metoclopramide Orion
(metoclopramide hydrochloride)

SE/H/1445/01/DC

This module reflects the scientific discussion for the approval of Metoclopramide Orion. The procedure was finalised at 2015-09-16. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Metoclopramide Orion, 10 mg, film-coated tablet, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Orion Corporation, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK and FI as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Primperan, 10 mg, tablet, authorised in SE since 1972, with Sanofi AB as marketing authorisation holder.

The reference product used in the bioequivalence study is Primperan, 10 mg, tablet, from SE with Sanofi AB as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

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, two-way crossover study conducted in 28 healthy volunteers, comparing Metoclopramide, 10 mg, tablet with Primperan, 10 mg, tablet under fasting conditions. The study was conducted at Accutest Research Lab, Ahmedabad, INDIA between 17th and 26th October 2013. Blood samples were collected pre-dose and up to 36 hours post-dose. The study design is considered acceptable. Plasma concentrations of metoclopramide 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%.
Based on the submitted bioequivalence study, Metoclopramide Orion is considered bioequivalent with Primperan.

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 (RMP), 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 Metoclopramide Orion.

Safety specification

Summary table of safety concerns as approved in RMP

Important identified risks	• Severe hypertensive events • Increased extrapyramidal reactions • Tardive dyskinesia • Hypersensitivity reactions • Worsening of existing gastrointestinal disorders • Hyperprolactinemia • Methaemoglobinaemia • Decreased effect when used concomitantly with levodopa and/or anticholinergic agents

Important potential risks	• Seizure risk in epileptics • Neuroleptic malignant 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

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

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
Important identified risks: • Severe hypertensive events • Increased extrapyramidal reactions • Tardive dyskinesia • Hypersensitivity reactions • Worsening of existing gastrointestinal disorders • Hyperprolactinemia • Methaemoglobinaemia • Decreased effect when used concomitantly with levodopa and/or anticholinergic agents	Information given in SmPC sections 4.3, 4.4, 4.5, 4.8 and 4.9. Other routine risk minimisation measures: • Prescription only medicine • Close monitoring through routine pharmacovigilance	None proposed.
Important potential risks: • Seizure risk in epileptics • Neuroleptic malignant syndrome	Information given in SmPC sections 4.3, 4.4 and 4.8. Other routine risk minimisation measures: • Prescription only medicine • Close monitoring through routine pharmacovigilance	None proposed.

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures

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 Metoclopramide Hydrochloride, NL/H/2418/001/MR. 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, Metoclopramide Orion, Film-coated tablet, 10 mg, is found adequate. There are no objections to approval of Metoclopramide Orion, 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 Metoclopramide Orion, Film-coated tablet, 10 mg was positively finalised on 2015-09-16.

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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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