Public Assessment Report

Scientific discussion

Moxalole
Powder for oral solution
(Macrogol 3350, sodium chloride, sodium hydrogen carbonate, potassium chloride)

DK/H/1199/001/DC

This module reflects the scientific discussion for the approval of Moxalole. The procedure was finalised on 12 June 2008. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

This assessment report concerns a generic version of Movicol, powder for oral solution approved through DCP with Denmark acting as RMS.

Based on the review of the data on quality, safety and efficacy, the application for Moxalole, in the treatment of

- Chronic constipation.
- Resolving faecal impaction, defined as refractory consitpation with faecal loading of the rectum and/or colon confirmed by physical examination of the abdomen and rectum.

was approved on 12 June 2008.

Macrogol 3350 is an osmotic acting laxative. Macrogol 3350 increases the stool volume, which triggers colon motility via neuromuscular pathways. The physiological consequence is an improved propulsive colonic transportation of the softened stools and a facilitation of the defecation. Electrolytes combined with macrogol 3350 are exchanged across the intestinal barrier with serum electrolytes and excreted in faecal water without net gain or loss of sodium, potassium and water.

The application is based 10(1) of Directive 2001/83/EC as amended. The brand leader is approved in all Member States involved in the procedure.

Essential similarity is claimed to Movicol, powder for oral solution 13.8 g registered in Sweden since 15.08.1996.
The active substances, macrogol 3350, sodium chloride, sodium hydrogen carbonate and potassium chloride are the same as in the originator product. The efficacy and safety profile is therefore considered identical.

No bioequivalence study has been performed since Macrogol 3350 undergoes virtually no absorption from the GI tract and passes unchanged through the gut and the composition of Moxalole is exactly the same as that of Movicol qualitatively and quantitatively. Both products dissolve rapidly and are taken after complete dissolution. In-vitro comparative studies are considered irrelevant.

II. QUALITY ASPECTS

II.1 Introduction

The finished product is presented as a powder for solution packed in sachets. The packaging contains 8, 10, 20, 30, 50 and 100 sachets.

The Excipients are: Acesulfam potassium (E950), lemon flavour.

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

II.2 Drug Substance

The Applicant's specification complies with the Ph. Eur. monograph for Macrogols.
The proposed re-test period of 24 months is justified.

Sodium chloride, potassium chloride and sodium hydrogen carbonate are common substances and are used as excipients in a large number of pharmaceutical products and are common ingredients of food. Consequently the information provided for each of these "salts" is limited for a drug substance.

The above "salts" are adopted by the Ph. Eur. The manufacturers' and the Applicant's specifications comply with Ph. Eur. monographs.

II.3 Medicinal Product

The chemical-pharmaceutical documentation and Quality Overall Summary presented are of sufficient quality in view of the present European regulatory requirements.

The development of the drug product has been described, the choice of excipients is justified and their functions explained.

The drug product specification covers appropriate parameters for this dosage form.

Validation of the analytical procedures has been presented. Batch analysis has been performed for one laboratory batch and two pilot scale batches. The batch analysis results meet the specification proposed.

The conditions used in the stability studies are according to ICH stability guideline. The control tests and specification for the drug product are adequately drawn up. The shelf-life accepted is: 24 *months / Store in the original package in order to protect from moisture*. For the reconstituted solution the shelf-life accepted is: *6 hours / refrigerator.*

III. NON-CLINICAL ASPECTS

Pharmacodynamic, pharmacokinetic and toxicological properties of Macrogol 3350/Sodium chloride/Potassium chloride/Sodium hydrogen carbonate in combination are well known. As Macrogol 3350/Sodium chloride/Potassium chloride/Sodium hydrogen carbonate is a widely used, well-known combination, no further studies are required and the applicant provides none. Overview based on literature review is, thus, appropriate.

The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate.

IV. CLINICAL ASPECTS

IV.1 Introduction

No specific clinical studies have been performed, as the application is submitted in accordance with Article 10(1) of Directive 2001/83/EEC as amended.

The Clinical overview on the clinical pharmacology, efficacy and safety is adequate.

Description of the Risk Management Plan (RMP) and the pharmacovigilance system
No Risk Management Plan other than documentation of pharmacovigilance system has been provided. For generics this is considered acceptable.
An adequate and detailed description of the pharmacovigilance system has been provided by the applicant.

IV.2 Pharmacokinetics

A comparison of bioequivalence of the two products has not been performed since Macrogol 3350 undergoes virtually no absorption from the GI tract and passes unchanged through the gut. The composition of Moxalole is exactly the same as that of Movicol qualitatively and quantitatively. Both products dissolve rapidly and are taken after complete dissolution. In-vitro comparative studies are considered irrelevant.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The presented overviews are adequate. The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The benefit risk is, therefore, considered to be positive.

The following commitments have been made during the procedure:

Drug substance

Macrogol 3350
S.6

- The Applicant commits to provide (not later than 1st August 2008) an updated specification (including IR as identification) for the primary packaging material concerning Macrogol 3350.

Sodium hydrogen carbonate
S.7

- The Applicant commits to test the drug substance prior to every use until the requested and acceptable stability results are generated.

Drug product:
P.3.5

- The Applicant commits to provide validation / evaluation data concerning three consecutive full-scale batches before market launch.

P.5.4

- The Applicant commits to provide batch analysis results concerning three consecutive full-scale batches before market launch.

P.8.2

- The Applicant commits to place the first three production scale batches on stability study cf. ICH.

- The Applicant commits to continue the on-going stability studies up to the proposed shelf-life for the batches 156-009, 156-010 and 156-011.

PSURs should be submitted every 3 years.
The next data lock point is 12.06.2011. The first PSUR should be submitted no later than 60 days after this date (11.08.2011).

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Update

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This module reflects the procedural steps and scientific information after the finalisation of the initial procedure.

	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
Repeat use procedure with AT, CY, CZ, EL, ES, FR, HU, IE, IS, LU, PL, PT, SI, SK	DK/H/1199/001/E/001	N	02.07.2009	30.09.2009	Approval	Y, Annex 1

ANNEX 1 – Repeat use procedure (DK/H/1199/001/E/001)

The present dossier has been updated with regard to approved variations and fulfilment of commitments following the finalisation of DK/H/1199/001/DC.

The Repeat use procedure started on 2 July 2009. There was no discussion in the CMD(h). Agreement between member states was reached during a written procedure. The concerned member states (AT, CY, CZ, EL, ES, FR, HU, IE, IS, LU, PL, PT, SI and SK), on the basis of the data submitted, considered that a marketing authorisation could be granted.
The repeat use procedure was finished on 30 September 2009.

The date for the first renewal will be: 12 June 2013. This is in line with the date of finalisation of the original procedure (12 June 2008).
The PSUR submission cycle is 3 years. PSURs will be submitted in accordance with the date of finalisation of the original procedure (12 June 2008).

The following post-approval commitments have been made during the original procedure and the repeat use procedure:

Drug substance

Sodium hydrogen carbonate
S.7

- The Applicant commits to test the drug substance prior to every use until the requested and acceptable stability results are generated.

Drug product:

P.5.4

- The Applicant commits to provide batch analysis results concerning three consecutive full-scale batches before market launch.

P.8.2

- The Applicant commits to place the first three production scale batches on stability study cf. ICH.
- The Applicant commits to continue the on-going stability studies up to the proposed shelf-life for the batches 156-009, 156-010 and 156-011.
- A variation will be submitted to update certificates.
- A variation will be submitted to update the dossier with new specification 3.2.P.5.1.
- A type II variation will be submitted mid November 2009 to update the SPC, PIL and labelling with agreed changes during the repeat use procedure.