LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Läkemedelsverket 2014-04-11

Public Assessment Report
Scientific discussion

Husk Lindroos, oral powder
(*Plantago ovata*, husk, powder)

Asp no: 2008-0636

This module reflects the scientific discussion for the approval of Husk Lindroos, oral powder. The procedure was finalised 16 December 2009. For information on changes after this date please refer to the module 'Update'.

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LAY SUMMARY

The Medical Products Agency (Läkemedelsverket, MPA) has granted W. Ratje Frøskaller Aps, Denmark, a marketing authorisation for the herbal medicinal product Husk Lindroos, oral powder. The product is available without prescription and can be bought from pharmacies and other outlets.

Husk Lindroos has an extensive medicinal use in the EU, primarily for treatment of habitual constipation. The active ingredient is the husks of *Plantago ovata* Forssk. (ispaghula, vitt loppfrö).

The Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA) has concluded that the active substance in Husk Lindroos has a well-established medicinal use with a recognised efficacy and acceptable level of safety.

The chemical/pharmaceutical quality of the product is acceptable and no new or unexpected safety concerns have been identified during the assessment. It was therefore decided that Husk Lindroos could be granted a marketing authorisation as a herbal medicinal product.

I. INTRODUCTION

W. Ratje Frøskaller Aps, Denmark, has applied for a marketing authorisation for Husk Lindroos, oral powder. The application was submitted under Article 10a Well-established use application of the Directive 2001/83 EC, as amended.
The application is a national application for Sweden.

The active substance is *Plantago ovata*, husk, powder.
For approved indications, see the Summary of Product Characteristics (SmPC).

Husk Lindroos, oral powder, was first authorised as a natural remedy in 1998. As a consequence of the new legislation regarding (traditional) herbal medicinal products the product was reclassified as a herbal medicinal product in 2009.

II. QUALITY ASPECTS

II.1 Introduction

Husk Lindroos is presented in the form of an oral powder consisting only of the active substance husk of *Plantago ovata* Forssk.

There are no excipients in the product.

All manufacturers involved in the production operate in accordance with EU-GMP, or where relevant, GACP or similar standards (Good Manufacturing Practise, respectively Good Agricultural and Collection Practice).

II.2 Drug Substance

The herbal substance *Plantago ovata* Forssk. seminis tegumentum complies with the monograph Ispaghula husk in the European Pharmacopoeia.

The plants used are cultivated in India. Relevant information on growing conditions and controls of the herbal substance (such as residues of heavy metals and pesticides as well as microbiological quality) has been provided.

The manufacturing process has been adequately described and satisfactory specifications have been provided for starting materials and solvents.

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

II.3 Medicinal Product

Husk Lindroos, oral powder contains no excipients.

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.

III. NON-CLINICAL ASPECTS

III.1 Introduction

The Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA) has issued a Community monograph on *Plantago ovata* Forssk. seminis tegumentum in 2006. In this monograph, it was concluded that the active substance in Husk Lindroos, ispaghula husk, has a well-established medicinal use with a recognised efficacy and acceptable level of safety in the Community in accordance with Directive 2001/83/EC.

The reader is referred to the Community monograph and the pertinent assessment report for details.

III.2 Pharmacology

The ispaghula husks are particularly rich in fibres and mucilages. According to the HMPC assessment report animal studies have shown laxative effects and effect on blood lipid levels.

III.3 Pharmacokinetics

No information available.

III.4 Toxicology

The non-clinical data on toxicology of ispaghula husk preparations are incomplete, but available data indicate no signals of toxicological concern. Adequate tests on reproductive toxicity, genotoxicity and carcinogenicity have not been published. Since the product is absorbing water it is not technically possible to test it in vitro.

III.5 Ecotoxicity/environmental risk assessment

Husk Lindroos is a herbal medicinal product. According to *Guideline on the environmental risk assessment of medicinal products for human use* (EMEA/CHMP/SW4447/00), herbal medicinal products are exempted from the obligation to present an environmental risk assessment due to the nature of their constituents.

III.6 Discussion on the non-clinical aspects

Ispaghula husks have been in medicinal use in the Community for a long period of time. The preparation in Husk Lindroos is recognised to have a well established medicinal use with an acceptable level of safety in the European Community.
No serious safety concerns have been identified.

IV. CLINICAL ASPECTS

IV.1 Introduction

The Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA) has issued a Community monograph on *Plantago ovata* Forssk. seminis tegumentum in 2006. In this monograph, it was concluded that the active substance in Husk Lindroos, ispaghula husk, has a well-established medicinal use with a recognised efficacy and acceptable level of safety in the Community in accordance with Directive 2001/83/EC.

The reader is referred to the Community monograph and the pertinent assessment report for details.

IV.2 Pharmacokinetics

According to the HMPC monograph, the fibres responsible for the therapeutic effect act locally in the gastrointestinal tract and are not absorbed. Metabolites, from fermentation and hydrolysis, can be absorbed but since such metabolites have no clinical significance pharmacokinetic studies are neither possible nor relevant.

IV.3 Pharmacodynamics

The mechanism of therapeutic action cannot be considered entirely clarified at present.
The husks are regarded as being the active constituent of Husk Lindroos.

According to the HMPC monograph, gut motility and transit rate can be modified by ispaghula husk through mechanical stimulation of the gut wall as a result of the increase in intestinal bulk by water and the decrease in viscosity of the luminal contents. When taken with a sufficient amount of liquid (at least 30 ml per 1 g of herbal substance) ispaghula husk produces an increased volume of intestinal contents due to its highly bulking properties and hence a stretch stimulus, which triggers defecation; at the same time the swollen mass of mucilage forms a lubricating layer, which makes the transit of intestinal contents easier.

Pharmacodynamic studies in humans have also shown effects on blood lipid levels, blood glucose levels and on diarrhoea.

IV.4 Clinical efficacy

In the assessment report pertaining to the Community monograph on Ispaghula husk an extensive review of clinical trials was presented. The assessment report concluded that the use of ispaghula husk according to the approved indications is well-established and more or less substantiated by its pharmacological effects.

IV.5 Clinical safety

The clinical safety documentation on Husk Lindroos indicates no signals of safety concern when used according to the SmPC.
Approval of Husk Lindroos as a herbal medicinal product with well-established use for the listed indications (please refer to IV.6) is therefore recommended with respect to clinical safety.

As no data on use in children are available, products containing *Plantago ovata* Forrsk. seminis tegumentum cannot be recommended for use in children below the age of 6 years.

Products containing *Plantago ovata* Forrsk. seminis tegumentum can be used during pregnancy and lactation.

There are no new signals of safety concern in the submitted product specific documentation relating to Husk Lindroos.

IV.6 Discussion on the clinical aspects

Husk Lindroos is a herbal medicinal product available without prescription with the following indications:

- Herbal medicinal product for the treatment of habitual constipation.
- Herbal medicinal product for the treatment of conditions in which easy defaecation with soft stool is desirable, e.g. in cases of painful defaecation after rectal or anal surgery, anal fissures, haemorrhoids or pregnancy.
- Herbal medicinal product as an adjuvant to diet in moderate hypercholesterolemia. Treatment requires medical supervision.
- Herbal medicinal product in patients to whom an increased daily fibre intake may be advisable e.g. as an adjuvant in diarrhoea and/or constipation associated with irritable bowel syndrome, when other causes for symptoms are excluded.

V. PRODUCT INFORMATION

The product information (Summary of Product Characteristics, Package Leaflet and labelling) has been assessed and accepted by the Medical Products Agency.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The adverse reactions reported during an extensive use of Ispaghula husk are no cause for safety concern. No new safety signals have been identified in the submitted product specific documentation relating to Husk Lindroos.

The benefit/risk ratio is considered positive and Husk Lindroos, oral powder is recommended for approval.

VII. APPROVAL

Husk Lindroos, oral powder was approved in the national procedure on 2009-12-16.

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Läkemedelsverket 2014-04-11

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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