LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Läkemedelsverket 2015-09-16

Public Assessment Report
Scientific discussion

Echinaforce comp oromucosal spray, solution

Echinacea purpurea **(L.) Moench (purple coneflower) herba recens, extract (3.5-6.4:1),**

Echinacea purpurea **(L.) Moench (purple coneflower) radix recens, extract (3.3-6.3:1)**

Salvia officinalis **L. (sage) folium recens, extract (1:2.5-4.3)**

Asp. No: 2014-0040

This module reflects the scientific discussion for the approval of Echinaforce comp, oromucosal spray, solution. The procedure was finalised at 16 June 2015. 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 Svenska Bioforce AB, Sweden, a traditional-use registration for the herbal medicinal product Echinaforce comp, oromucosal spray, solution. This product is available without prescription and can be bought from pharmacies and other outlets.

Echinaforce comp is traditionally used for the relief of sore throat associated with common cold. The indication in Swedish is ”Traditionellt växtbaserat läkemedel använt för lindring av halsont i samband med förkylning. Indikationerna för ett traditionellt växtbaserat läkemedel grundar sig uteslutande på erfarenhet av långvarig användning.”

There are three active ingredients: two extracts from fresh herb and root of *Echinacea purpurea* (L.) Moench (purple coneflower, röd solhatt) respectively, and one extract from fresh leaves of *Salvia officinalis* L. (sage, salvia). This registration is based exclusively upon evidence of traditional use of purple coneflower and sage as herbal medicinal products and not upon data generated from clinical trials. For traditional herbal medicinal products there is no requirement to scientifically prove the effect; adequate evidence of traditional use is sufficient.

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 Echinaforce comp could be registered as a traditional herbal medicinal product.

I. INTRODUCTION

Svenska Bioforce AB has applied for a traditional-use registration for Echinaforce comp, oromucosal spray, solution. The application was submitted under Article 16a traditional use registration for herbal medicinal product of the Directive 2001/83 EC, as amended.
The application is a national application for Sweden.

The active substances are:
Echinacea purpurea (L.) Moench, fresh herb, soft extract (3.5-6.4:1), ethanol 87 % (v/v)

Echinacea purpurea (L.) Moench, fresh root, soft extract (3.3-6.3:1), ethanol 86 % (v/v)

Salvia officinalis L., fresh leaf, liquid extract (1:2.5-4.3), ethanol 84% (v/v)

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Echinaforce comp is presented in the form of an oromucosal spray.

Each ml of the oromucosal spray contains 69,1 mg extract from *Echinacea purpurea* herba recens, 3,6 mg extract from *Echinacea purpurea* radix recens and 430 mg extract from *Salvia officinalis* folium recens. For the manufacture of 1 ml oromucosal spray, 245-440 mg of fresh herb of purple coneflower, 12-23 mg of fresh roots of purple coneflower and 100-175 mg of fresh sage leaves are used.
The extraction solvent is ethanol and the extracts contain 65% (v/v), 65% (v/v) and 68% (v/v) ethanol respectively.

The excipients are:
Sorbitol (liquid, non-cristal.), ethanol, soy lecithin, sucrose laurate (E473) and peppermint oil.
The average ethanol content in the oromucosal spray is 43.5% (v/v).

The oromucosal spray is available in 30 ml brown glass bottles with a spray pump (made of polyethylene).

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

II.2 Drug Substance

The herbal substances *Echinacea purpurea* fresh herb, *Echinacea purpurea* fresh root and *Salvia officinalis* fresh leaves are controlled using in-house specifications based on the European pharmacopoeia (Ph. Eur.) monographs for the same dried substances.

The plants used are cultivated in Central Europe. 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 fresh plant material is cut (the roots also washed) before being extracted with ethanol. Both extracts from purple coneflower are made separately, but later they are mixed to an intermediate product in the ratio 95:5 (herb tincture:root tincture).

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

The active substances' specifications include relevant tests and the limits for impurities have been justified. The analytical methods applied are suitably described and validated.

Stability studies under ICH conditions have been conducted.

II.3 Medicinal Product

Echinaforce comp, oromucosal spray, is formulated using excipients described in the Ph. Eur., except for liquid sorbitol, sucrose laurate and soy lecithin which are controlled according to acceptable in-house specifications. All raw materials used in the product are safe with view to possible TSE/BSE risk, as they are all from non-animal and non-human sources.

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 AND CLINICAL ASPECTS

III.1 Introduction

The Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA) has not elaborated any Community monograph on the fixed combination of purple coneflower (*Echinacea purpurea*, fresh herb and fresh root) and sage (*Salvia officinalis*, fresh leaf) in Echinaforce comp. However, there are individual Community monographs on all three herbal substances in dried form. In addition, the applicant has collected relevant additional information from the literature that has been evaluated by the MPA.

III.2 Non-clinical aspects

The applicant has collected available information from the literature in the areas of non-clinical pharmacology and toxicology. This information has been assessed by the MPA and no signals of non-clinical safety concern have been identified. The exact mechanism of action of the active substances contained in Echinaforce comp in relation to its traditional medicinal use cannot be considered clarified.

A product specific study on mutagenic activity has been performed. The extracts have shown not to be mutagenic in Ames test.

Based on the non-clinical information, both from the literature and the product specific study, no objections are raised to the approval of purple coneflower herb and root, and sage leaf as active ingredients in a traditional herbal medicinal product.

III.3 Ecotoxicity/environmental risk assessment

Echinaforce comp is a traditional herbal medicinal product. According to "Guideline on the environmental risk assessment of medicinal products for human use" (EMEA/CHMP/SWP/4447/00), (traditional) herbal medicinal products are exempted from the obligation to present an environmental risk assessment due to the nature of their constituents.

III.4 Clinical aspects

Results of clinical trials concerning clinical efficacy and safety are not required for the registration of a traditional herbal medicinal product.

III.5 Traditional use

The applicant has provided a bibliographic review which shows sufficient evidence for the medicinal use of *Echinacea purpurea,* herba and radix, and *Salvia officinalis,* folium throughout a period of at least 30 years, including at least 15 years within the Community. The combination is mainly used in form of oral dosage forms for the relief of sore throat associated with common cold. The recommended dosage of Echinaforce comp is in the same range as the posology listed in the individual HMPC monographs and in the literature.
The product itself has been registered as a traditional herbal medicinal product, under the Article 16a of the Directive 2001/83 EC as amended, in UK, Spain, Slovenia and Croatia.

III.6 Clinical safety

Conventional clinical safety data are virtually absent. However, longstanding medicinal use and experience of *Echinacea purpurea,* herba and radix, and *Salvia officinalis,* folium, has been documented within the Community. During this time, no clinical signals that *Echinacea purpurea,* herba and radix, and *Salvia officinalis,* folium are harmful under normal conditions of use have been identified.

As no data on use in children are available, products containing *Echinacea purpurea,* herba and radix, and *Salvia officinalis,* folium *cannot* be recommended for use in children below the age of 18 years.

Due to lack of safety data, the use of products containing *Echinacea purpurea,* herba and radix, and *Salvia officinalis,* folium during pregnancy and lactation is not recommended.

Based on the clinical safety information available, no objections are raised to the approval of Echinaforce comp as a traditional herbal medicinal product.

IV. PRODUCT INFORMATION

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

V. OVERALL CONCLUSION, RISK ASSESSMENT AND RECOMMENDATION

For Echinaforce comp, oromucosal spray, solution, the handling, manufacture and quality control of raw materials, active substance and finished product are in line with GMP and pharmacopoeial requirements. The applicant has shown that the chemical/pharmaceutical quality is acceptable and can confirm that the process is under control and ensure both batch reproducibility and compliance with the product specification.

The Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA) has not elaborated any Community monograph on the fixed combination of fresh purple coneflower herb and root, and fresh sage leaf, but there are individual Community monographs on all three herbal substances in dried form. The applicant has provided evidence that Echinaforce comp has had a medicinal use for at least 30 years, including at least 15 years within the Community.

No signals of preclinical or clinical safety concern have been identified under normal conditions of use.

Echinaforce comp, oromucosal spray, solution, can be recommended for registration as a traditional herbal medicinal product.

VI. APPROVAL

Echinaforce comp, oromucosal spray, solution, was approved in the national procedure on 2015-06-16.

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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