LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Echinaforce, oral drops solution

***Echinacea purpurea* (L.) Moench (purple coneflower) herba recens, extract**
and
***Echinacea purpurea* (L.) Moench (purple coneflower) radix recens, extract**

Asp. No: 2008-1040

This module reflects the scientific discussion for the approval of Echinaforce, oral drops, solution. The procedure was finalised at 7 October 2009. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se

LAY SUMMARY

The Medical Products Agency (Läkemedelsverket) has granted Svenska Bioforce AB, Sweden, a traditional-use registration for the herbal medicinal product Echinaforce oral drops, solution. This product is available without prescription and can be bought from pharmacies and other outlets.

Echinaforce is traditionally used for the relief of symptoms of common cold. The active ingredients are two ethanolic extracts from fresh roots respectively fresh herb of *Echinacea purpurea* (L.) Moench (purple coneflower, röd solhatt). This registration is based exclusively upon evidence of traditional use of *Echinacea purpurea* as a herbal medicinal product 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, oral drops solution, could be registered as a traditional herbal medicinal product.

I. INTRODUCTION

Svenska Bioforce AB has applied for a traditional use registration for Echinaforce, oral drops, 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, liquid extract (1:2.0-3.6), ethanol 57 % (m/m)
Echinacea purpurea (L.) Moench fresh root, liquid extract (1:1.9-3.8), ethanol 57 % (m/m)

Echinaforce, oral drops, solution, was first authorised as a natural remedy in 2004. With the new legislation regarding (traditional) herbal medicinal products the product was reclassified as a traditional herbal medicinal product in 2009.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Echinaforce is presented in the form of oral drops, solution, each ml containing 860 mg of the active substance *Echinacea purpurea* (L.) Moench fresh herb, liquid extract (1:2.0-3.6), ethanol 57 % (m/m), corresponding to 340 mg of fresh herb of purple coneflower, and 45 mg of the active substance *Echinacea purpurea* (L.) Moench fresh root, liquid extract (1:1.9-3.8), ethanol 57 % (m/m), corresponding to 18 mg of fresh root of purple coneflower.

The product contains no excipients except for the ethanol and water contained in the extracts.

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

II.2 Drug Substance

The herbal substances *Echinacea purpurea* (L.) Moench fresh herb and *Echinacea purpurea* (L.) Moench fresh root are controlled using in-house monographs based on the 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 plant material is cut (the roots also washed) before being extracted with ethanol. Both extracts are made separately but later mixed to an intermediate product in the ratio 95:5 (herb liquid extract:root liquid extract).

The manufacturing process has been adequately described and satisfactory specifications have been provided for starting materials and the 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, oral drops, solution, is formulated using no excipients except for the ethanol and water contained in the extracts. Ethanol and water are described in the current Ph. Eur. All raw materials used in the product are safe with view to possible TSE/BSE risk.

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 SmPC.

III. NON-CLINICAL AND CLINICAL ASPECTS

III.1 Introduction

The Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA) has issued a Community monograph on *Echinacea purpurea* herba and *Echinacea purpurea* radix. The extracts in Echinaforce, oral drops, solution are partially covered by the HMPC monographs. The reader is referred to the Community monographs and the pertinent assessment reports for details.

The product range Echinaforce has been in use in the Community for more than 50 years.

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 extracts from *Echinacea purpurea* herb respectively root in relation to their traditional medicinal use cannot be considered clarified.

A product/extract specific study on mutagenic activity has been performed. The extract has been 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 ethanolic extracts of *Echinacea purpurea* as active ingredient in a traditional herbal medicinal product.

III.3 Ecotoxicity/environmental risk assessment

Echinaforce 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 medicinal use of *Echinacea purpurea,* herb and root has a long tradition exceeding 50 years in the Community. It is mainly used for the relief of symptoms of common colds. The recommended dosage of Echinaforce is in the same range as the ones used traditionally and listed in the literature.

The applicant has provided a bibliographic review which shows sufficient evidence for the medicinal use of *Echinacea purpurea* throughout a period of at least 30 years, including at least 15 years within the Community. Hence, the requirement of traditional use according to Directive 2004/24/EC is considered fulfilled.

III.6 Clinical safety

The safety profile of Echinaforce, oral drops, solution is well established both from clinical studies and from its use for over 50 years as a marketed medicinal product in many countries world-wide with usage by many millions of patients.

In the assessment report pertaining to the Community monograph on *Echinacea purpurea,* herb, hypersensitivity to plants of the Asteraceae family is mentioned as well as severe immune reactions for atopic patients. As with all immunostimulants, *Echinacea* is not recommended in cases of progressive systemic disorders and autoimmune diseases immunodeficiencies, immunosuppression and diseases of the white blood cell system such as tuberculosis, leukoses, collagenoses, multiple sclerosis, AIDS or HIV-infections
The majority of adverse events reported are related to hypersensitivity reactions like rashes including urticaria.

Information about the large sales volumes of products containing the Echinaforce extracts and a very long history of traditional use indicate that Echinaforce, oral drops, solution is generally safe.

As no safety data on use in children are available, products containing *Echinacea purpurea,* herb and/or root *cannot* be recommended for use in children aged 1 to 12 years. The use is contraindicated for children below the age of 1 year.

Due to lack of safety data, the use of products containing *Echinacea purpurea,* herb and/or root during pregnancy and lactation is not recommended.

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

IV. OVERALL CONCLUSION, RISK ASSESSMENT AND RECOMMENDATION

For Echinaforce, oral drops, 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 ensures both batch reproducibility and compliance with the product specification.

The applicant has provided evidence that the extracts have 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, oral drops, solution, can be recommended for registration as a traditional herbal medicinal product.

V. APPROVAL

Echinaforce, oral drops, solution, was approved in the national procedure on 7 October 2009.

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

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)

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se