IPAR

HEALTH PRODUCTS REGULATORY AUTHORITY

PUBLIC ASSESSMENT REPORT FOR A TRADITIONAL HERBAL MEDICINAL RODUCT FOR HUMAN USE

ECHINACE TABLETS
ECHINACEA PURPUREA ROOT DRY EXTRACT

TR 1725/1/1
TR HOLDER SONA NUTRITION LTD

JULY 2014

I INTRODUCTION

Specific provisions were introduced for traditional herbal medicinal products (THMPs) in accordance with the Traditional Herbal Medicinal Products Directive (2004/24/EC). The national regulations, the Medicinal Products (Control of Placing on the Market) Regulations 2007 (S.I. No. 540 of 2007) which implement this Directive came into force on 23rd July 2007. Consequently HPRA has established the Traditional Herbal Medicinal Products Registration Scheme.

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a Certificate of Traditional Use Registration for a specific traditional herbal medicinal product for human use. It is made available by HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of EC Directive 2001/83/EC, as amended by Directive 2004/27/EC and Directive 2004/24/EC. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by HPRA leading to the approval of the traditional herbal medicinal product for marketing in Ireland.

Based on the review of the data on quality, safety and traditional use, HPRA has granted Sona Nutrition Limited a Certificate of Traditional Use Registration for Echinace Tablets, containing *Echinace purpurea* root dry extract.

This application was submitted as a standard application according to Article 16a of Directive 2001/83/EC, as amended, as part of the Traditional Herbal Medicinal Product Registration Scheme.

The Summary of Product Characteristics (SmPC) for this traditional herbal medicinal product is available on HPRA's website.

II QUALITY ASPECTS

This application is for Echinace Tablets. The active ingredient of Echinace Tablets is a dry extract obtained from *Echinacea purpurea* radix (Purple Coneflower Root).

Each film-coated tablet contains 127.0 mg of extract (as dry extract) from *Echinacea purpurea* radix (6-7:1) (equivalent to 762 mg - 889 mg of *Echinacea purpurea* (L.) Moench radix) (Purple coneflower root).

II.1 S.1 Herbal Substance

The herbal substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification have been provided.

II.2 S.2 Herbal preparation

The herbal preparation is *Echinacea purpurea* root dry extract and is manufactured in accordance with the principles of good manufacturing practice (GMP).

The herbal preparation specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification have been provided.

II.3 Medicinal product

P.1 Composition

The product is a pale yellow, oval, biconvex film-coated tablet.

Each film-coated tablet contains 127.0 mg of extract (as dry extract) from *Echinacea purpurea* radix (6-7:1) (equivalent to 762 mg - 889 mg of *Echinacea purpurea* (L.) Moench radix) (Purple coneflower root).
The tablets also contain Maltodextrin, Calcium Hydrogen Phosphate Dihydrate, Microcrystalline Cellulose, Croscarmellose Sodium, Magnesium Stearate, Colloidal Anhydrous Silica, Hypromellose, Talc and Yellow Dispersion (containing Hypromellose, Titanium Dioxide, E171 and Yellow Iron Oxide, E172).

P.2 Pharmaceutical Development

The product is an established pharmaceutical form and its development is adequately described.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of GMP at suitably qualified manufacturing sites.

The manufacturing process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients/*Ancillary Substances)*

All ingredients comply with Ph. Eur. except for the yellow dispersion which is adequately controlled by the manufacturer’s specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for tablets, and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The product is presented in a PVC/PVDC blister pack with aluminium foil.

Evidence has been provided that all packaging materials comply with appropriate EU legislation for use with foodstuffs.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines demonstrating the stability of the product for 2 years when stored below 25 °C in the original container.

II.4 Conclusion on quality

The important quality characteristics of the product are well-defined and controlled. Satisfactory pharmaceutical documentation has been provided, assuring consistent quality of Echinace Tablets.

III NON-CLINICAL ASPECTS

Echinace is a traditional herbal medicinal product as defined by Article 16a(1) of Directive 2001/83/EC as amended.

No new preclinical studies have been submitted. Given the type of application and limited data available, it is not possible to assess if the safety package for the phytochemical constituents of Echinace are acceptable to the standards of today's GLP and safety testing requirements.

An expert report on safety has been provided which includes an appropriate review of the available literature. Overall the information presented demonstrating traditional use is considered to be acceptable and the lack of provision of a complete standard safety package is in line with the EMA 'Guideline on Non-clinical Documentation for Herbal Medicinal Products in Applications for Marketing Authorisation (bibliographical and mixed applications) and in Applications for Simplified Registration' (EMEA/HMPC/32116/05). In view of the absence of genotoxicity data the applicant is required to submit this data within two years of the granting of a certificate of registration.

An environmental risk assessment is not required for herbal medicinal products according to guidance CPMP/SWP/4447/00.

IV CLINICAL ASPECTS

This is a national application submitted by Sona Nutrition Ltd under Article 16a of Directive 2001/83/EC, as amended.

Echinace is a traditional herbal medicinal product used to relieve common cold and flu-like symptoms in adolescents and adults, exclusively based on long-standing use.

IV.1 Clinical Efficacy

There is no requirement under the Traditional Herbal Registration scheme to prove scientifically that the product is efficacious, the registration is based exclusively upon the long-standing use of Echinace as a traditional herbal medicine and not upon data generated from clinical trials.

Article 16c1(c) of Directive 2001/83/EC requires the applicant to provide bibliographic or expert evidence to show that the medicinal product in question, or a corresponding product, has been in medicinal use throughout a period of at least 30 years, including at least 15 years within the Community. With regard to this traditional use data, the requirements of Article 16c1(c) have been met.

The efficacy of this traditional herbal medicinal product is plausible on the basis of long standing use and experience.

The indication proposed for Echinace is in line with traditional indications recorded and hence, compatible with the requirements of the Traditional Herbal Medicinal Products Directive 2004/24/EC.

IV.2 Clinical Safety

In accordance with Article 16c1(d) the applicant has provided a bibliographic review of the safety data together with an expert report.

Echinace is intended for oral short-term use only. The recommended dosage should not be exceeded.

If high temperature occurs, if symptoms worsen or persist for more than 10 days, it is recommended that a qualified healthcare professional e.g. a doctor or pharmacist be consulted.

Echinace should not be used in known cases of allergy to Echinacea, to plants of the Asteraceae (Compositae) family or to any of the excipients.

The use in children below 12 years of age is not recommended because a safe use has not been sufficiently documented.

Echinacea can trigger allergic reactions (E.g. rash, hives, Stevens-Johnson Syndrome, swelling of the skin, difficulty breathing, asthma and anaphylactic shock) in allergy-prone patients.

It is recommended that patients do not take this product if they are taking other medicines which affect their immune system.

There is limited information about the use of Echinace tablets in pregnant women. In the absence of enough information, the use in pregnancy and breast-feeding is not recommended.

Because of its immunostimulating activity, Echinacea should not be used in cases of progressive systemic diseases (tuberculosis, sarcoidosis), autoimmune diseases (e.g. collagenoses, multiple sclerosis), immunodeficiencies (e.g. HIV infection, AIDS), immunosuppression (e.g. chemotherapy, history of organ or bone marrow transplant), diseases of the white blood cell system (e.g. agranulocytosis, leukaemias) and allergic diatheses (e.g. urticaria, atopic dermatitis, asthma).

An association with some autoimmune diseases (E.g. multiple sclerosis, erythema nodosum, low blood platelet count, Evans Syndrome, Sjögren syndrome with kidney dysfunction) has also been reported. A decrease in the number of white blood cells may occur in long-term use of Echinacea (more than 8 weeks).

No studies on the effects on the ability to drive and use machines have been performed with Echinace.

There have been no cases of overdose reported with Echinacea products.

In conclusion, this product proves not to be harmful in the specified conditions of use, based on the review of safety data, expert report and additional data provided.

IV.3 Pharmacovigilance

It should be noted that in accordance with Article 16g of Directive 2001/83/EC, as amended, the pharmacovigilance requirements described in Articles 101- 108 of Directive 2001/83/EC, as amended, also apply in respect of traditional herbal medicinal products.

V OVERALL CONCLUSIONS

The important quality characteristics of the product are well-defined and controlled. Satisfactory pharmaceutical documentation has been provided, assuring consistent quality of Echinace Tablets.

HPRA, on the basis of the data submitted, considered that Echinace Tablets demonstrated adequate evidence of traditional use for the approved indication(s) and no new preclinical or clinical safety concerns have been identified.

A Certificate of Traditional Use Registration for Echinace Tablets is granted.

VI REVISION DATE

Deember 2014

VII UPDATES

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
B.II.f.1 b) 1. – Change in the shelf life of the finished product – extension of the shelf-life of the finished product as packed for sale (supported by real time data) from 2 to 3 years.	Not applicable (National variation)	Section 6.3 of the SPC: 6.3 Shelf life 3 years.		17th December 2014 (variation approved)