IPAR

Public Assessment Report for a
Traditional Herbal Medicinal Product
for Human Use

Natures Aid Echineeze Echinacea tablets
Echinacea purpurea root extract

TR0126/311/001
TR Holder Clonmel Healthcare Ltd

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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, the Health Products Regulatory Authority (HPRA) has established the Traditional Herbal Medicinal Products Registration Scheme.

The Public Assessment Report reflects the scientific conclusion reached by the 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 the 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 the 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, the HPRA has granted Clonmel Healthcare Limited a Certificate of Traditional Use Registration for Natures Aid Echineeze Echinacea Tablets, containing a dry extract of *Echinacea purpurea* root.

This application is for a traditional herbal medicinal product as defined by Article 16a(1) of Directive 2001/83/EC as amended and was submitted 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 the HPRA's website.

II. QUALITY ASPECTS

This application is for Natures Aid Echineeze Echinacea Tablets. The active ingredient of Natures Aid Echineeze Echinacea Tablets is obtained from *Echinacea purpurea* (L.) Moench, radix (Purple coneflower root).

II.1 S.1 Herbal Substance

The herbal substance is *Echinacea purpurea* (L.) Moench, radix (Purple coneflower root), described in the European Pharmacopoeia, and is produced in accordance with the principles of good agricultural and collection practice (GACP).

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 a dry extract of *Echinacea purpurea* (L.) Moench, radix (Purple coneflower root), 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 composition of the medicinal product is stated in sections 2 and 6.1 of the SmPC. A description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

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.

P.5 Control of the 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(s) have been provided and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the packaging materials comply with Ph. Eur. and/or EU legislation on materials intended 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 and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

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 Natures Aid Echineeze Echinacea Tablets.

III. NON-CLINICAL ASPECTS

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).

An initial Ames test submitted reported a positive mutagenic finding associated with salmonella strain TA102 in the presence of S9 metabolic activation. This was not evident when a non-GLP test was repeated on the same strain in a separate facility. Following a round of consultation with the applicant and a robust assessment of the available data, it is accepted that the non-GLP elements of the repeated study did not adversely affect the validity of the data generated. It is accepted that the totality of the data indicate Echinacea purpurea(L.) Moench root is not mutagenic.

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

IV. CLINICAL ASPECTS

Natures Aid Echineeze Echinacea Tablets is a traditional herbal medicinal product used to relieve common cold and flu-like symptoms, exclusively based on long-standing use. This product is indicated for use in adults and adolescents over 12 years.

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 longstanding use of Natures Aid Echineeze Echinacea Tablets 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 Natures Aid Echineeze Echinacea Tablets 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.

Natures Aid Echineeze Echinacea Tablets 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.

Natures Aid Echineeze Echinacea Tablets 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 Natures Aid Echineeze Echinacea 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 extracts 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. oncological cytostatic therapy, 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 Natures Aid Echineeze Echinacea Tablets

There have been no cases of overdose reported with Natures Aid Echineeze Echinacea Tablets

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 Natures Aid Echineeze Echinacea Tablets.

The HPRA, on the basis of the data submitted, considered that Natures Aid Echineeze Echinacea Tablets demonstrated adequate evidence of traditional use for the approved indication(s) and no new non-clinical or clinical safety concerns have been identified.

A Certificate of Traditional Use Registration for Natures Aid Echineeze Echinacea Tablets is granted.

VII. UPDATES

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
New Herbal	N/A	SPC Sections 1 to 9	14th October 2022	13th October 2027