IPAR

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

TR Holder

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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 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 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 NBTY Europe Ltd a Certificate of Traditional Use Registration for Holland & Barrett Echinacea Cold and Flu Hard Capsules, containing Dry extract of *Echinacea purpurea* (purple coneflower) root.

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 the HPRA's website.

II. QUALITY ASPECTS

This application is for Holland & Barrett Echinacea Cold and Flu Hard Capsules. The active ingredient of Holland & Barrett Echinacea Cold and Flu Hard Capsules is a dry extract obtained from the root of *Echinacea purpurea (purple coneflower)*.

Each hard capsule contains 140 mg of extract (as dry extract) from *Echinacea purpurea* root (equivalent to 838 mg –1117 mg of *Echinacea purpurea* (L.) Moench, root).

II.1 S.1 Herbal Substance

The herbal substance, *Echinacea purpurea radix* (Purple Coneflower root), is described in the European Pharmacopoeia. The herbal substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.2 S.2 Herbal preparation

The herbal preparation is a dry extract from *Echinacea purpurea* (L.) Moench, 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 has 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 standard. The manufacturer has extensive experience and has committed to carry out full process validation on commercial batches.

P.4 Control of Other Substances (Excipients)

All ingredients comply with Ph. Eur. or are adequately controlled by the manufacturer's specifications.

P.5 Control of Finished Product

The Finished Product Specification is satisfactory 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 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 components comply with the relevant EU legislation requirements 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 Holland & Barrett Echinacea Cold and Flu Hard Capsules.

III. NON-CLINICAL ASPECTS

Holland & Barrett Echinacea Cold and Flu Hard Capsules 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. An expert report on safety has been provided which includes an appropriate review of the available literature. No safety concern was identified. Overall, the information presented demonstrating traditional use is acceptable and thus the lack of provision of a complete standard safety package is acceptable and 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 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 NBTY Europe Ltd under Article 16a of Directive 2001/83/EC, as amended.

Holland & Barrett Echinacea Cold and Flu Hard Capsules is a traditional herbal medicinal product used to relieve common cold and flu-like symptoms in adults and adolescents over 12 years, exclusively based upon 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 longstanding use of Holland & Barrett Echinacea Cold and Flu Hard Capsules 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 Holland & Barrett Echinacea Cold and Flu Hard Capsules 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.

This product is indicated for short-term use only and the recommended dose should not be exceeded.
This product should not be used for more than 10 days. If symptoms worsen, persist or if new symptoms develop or high fever occurs, a doctor or pharmacist should be consulted.
This product should not be used by those who are allergic to Echinacea purpurea, to plants of the daisy family or to any of the ingredients of this product.

Because of their immune-modulatory activity, Echinacea extracts must not be used in cases of progressive systemic disorders (Tuberculosis sarcoidosis), autoimmune diseases (e.g. collagenosis, multiple sclerosis), immunodeficiencies (e.g. HIV infection, AIDS), immunosuppression (e.g. chemotherapy, history of organ or bone marrow transplant) and diseases of the white blood cell system (e.g. agranulocytosis, leukaemias).

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

There is a possible risk of anaphylactic reactions in atopic patients. Atopicpatients should consult a qualified healthcare professional e.g. a doctor orpharmacist before using Echinacea.

This product should not be used at the same time as other medications that affect the immune system.
There are no or limited amount of data from the use of *Echinacea purpurea* root in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3).
Holland and Barrett Echinacea Cold and Flu Hard Capsules is not recommended during pregnancy and in women of child-bearing potential not using contraception.

There is insufficient information on the excretion of *Echinacea purpurea* (L.)/metabolites in human milk. A risk to newborns/infants cannot be excluded. Holland & Barrett Echinacea Cold and Flu Hard Capsules should not be used during breast-feeding.
No studies on the effect on the ability to drive and use machines have been performed with this product.

Allergic reactions of the following nature may occur with Echinacea products:

- Anaphylactic shock (a life-threatening allergic reaction)
- Bronchospasm with obstruction (difficulty breathing)
- Asthma
- Urticarial rash (Hives)
- Angioedema of the skin (Swelling of the skin)
- Steven-Johnson Syndrome

Association with autoimmune diseases (multiple sclerosis, erythema nodosum, immune thrombocytopaenia, Evans Syndrome, Sjogren's syndrome with renal tubular disfunction) has been reported for Echinacea products.

A low white blood cell count may occur in long-term use of Echinacea (more than 8 weeks).

There have been no cases of overdose with Echinacea reported.

The frequency of the listed side effects is not known (cannot be estimated from the available data).

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 Holland & Barrett Echinacea Cold and Flu Hard Capsules.
The HPRA, on the basis of the data submitted, considered that Holland & Barrett Echinacea Cold and Flu Hard Capsules demonstrated adequate evidence of traditional use for the approved indication and no new preclinical or clinical safety concerns have been identified.
A certificate of traditional use registration for Holland & Barrett Echinacea Cold and Flu Hard Capsules is granted.

VI. REVISION DATE

February 2021

VII. UPDATES

Procedure number	Product Information affected	Date of start of procedure	Date of end of procedure	Approval/non approval
CRN00C3J5 TR Transfer	SPC section 7, 8 Package Leaflet New TR Holder: Holland & Barrett Limited, Cedar Drive, Dublin Airport Logistics Park, Saint Margarets, Co Dublin, K67 E0C5, Ireland New TR number: TR23157/007/001	26/02/2021	26/02/2021	Approved