IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

CONTENTS

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 Irish Botanica a Certificate of Traditional Use Registration for Irish Botanica Echinacea Oral Liquid, containing a tincture of dried *Echinacea purpurea* (L.) Moench 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 Irish Botanica Echinacea Oral Liquid. The active ingredient of Irish Botanica Echinacea Oral Liquid is an ethanolic tincture obtained from the dried root of *Echinacea purpurea* plant.

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 an ethanolic tincture of dried *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 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.

P.3 Manufacture of the Product
The product is manufactured in accordance with the principles of GMP at a suitably qualified manufacturing site.
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 Liquid Preparations for Oral Use 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 considered to be sufficiently validated.
Batch analytical data 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 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 EU food contact legislation requirements.

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 Irish Botanica Echinacea Oral Liquid.

III. NON-CLINICAL ASPECTS

No new non-clinical studies have been submitted.

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

IV. CLINICAL ASPECTS

Irish Botanica Echinacea Oral Liquid is a traditional herbal medicinal product used in adults to
relieve common cold and flu-like symptoms, 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 longstanding use of Irish Botanica Echinacea Oral Liquid 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 Irish Botanica Echinacea Oral Liquidis 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 intended for short-term use only. The recommended dose should not be exceeded. If a high temperature occurs or if symptoms persist, worsen or do not improve after 10 days use of Irish Botanica Echinacea Oral Liquid, a qualified healthcare professional e.g. a doctor or pharmacist should be consulted.

The use of Irish Botanica Echinacea Oral Liquid, in children and adolescents below 18 years of age is not recommended because a safe use has not been sufficiently documented.

It is recommended that Irish Botanica Echinacea Oral Liquid, should not be used in cases of known allergy to the active substance, to plants of the Asteraceae (Compositae) family or to any of the excipients.

This medicinal product contains 45% v/v ethanol (alcohol), i.e. up to 0.9g per dose, equivalent to approximately 23ml beer, or 9ml wine per dose. This may be harmful for those suffering from alcoholism. The alcohol content should be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease, or epilepsy.

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.

Because of their effects on the immune system, Echinacea extracts must not be used in cases of progressive systemic disorders (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) and diseases of the white blood cell system (e.g. agranulocytosis, leukaemias).

This product should not be used at the same time as other medications affecting the immune system. This product contains alcohol, and should therefore be avoided in patients taking other medications known to interact with alcohol (e.g. metronidazole).

No studies on the effect of this product on the ability to drive or use machinery have been performed. This product contains alcohol and overdose of this product may result in alcohol intoxication.

There is limited information about the use of in pregnant women. In the absence of enough information, the use of Irish Botanica Echinacea Oral Liquid, in pregnancy and breast-feeding is not recommended.

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.

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 Irish Botanica Echinacea Oral Liquid.
The HPRA, on the basis of the data submitted, considered that Irish Botanica Echinacea Oral Liquid demonstrated adequate evidence of traditional use for the approved indication and no new non-clinical or clinical safety concerns have been identified.
A Certificate of Traditional Use Registration for Irish Botanica Echinacea Oral Liquid is granted.