IPAR

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

Strepsils Herbal Dry Cough Syrup
Ribwort plantain dry extract

TR0979/088/001
TR Holder Reckitt Benckiser Ireland Limited

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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 Reckitt Benckiser Ireland Limited a Certificate of Traditional Use Registration for Strepsils Herbal Dry Cough Syrup containing a dry extract of ribwort plantain.

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.

Name of the product	Strepsils Herbal Dry Cough Syrup
Name of the active substance	Dry extract of ribwort plantain
Pharmaceutical form	Syrup
Registration Number in Ireland	TR0979/088/001
Registration Holder	Reckitt Benckiser Ireland Limited 7 River Walk Citywest Business Campus Dublin 24, D24 H2CE Ireland

II. QUALITY ASPECTS

This application is for Strepsils Herbal Dry Cough Syrup. The active ingredient of Strepsils Herbal Dry Cough Syrup is obtained from ribwort plantain.

II.1 S.1 Herbal Substance

The herbal substance is ribwort plantain, 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 ribwort plantain 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 has been validated according to relevant European/ICH guidelines and the process is considered to be sufficiently validated.

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

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

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 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 Strepsils Herbal Dry Cough Syrup.

III. NON-CLINICAL ASPECTS

The product is a traditional herbal medicinal product as defined by Article 16a(1). An expert report on safety has been provided which includes an appropriate review of the available literature. A single new nonclinical study has been submitted in relation to genotoxicity testing. This study was performed to GLP and indicated that Strepsils Herbal Dry Cough Syrup is not mutagenic.

Given the type of application and limited data available, it is not possible to assess if the safety package for the phytochemical constituents of Strepsils Herbal Dry Cough Syrup are acceptable to the standards of today's GLP and safety testing requirements. However, 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 environmental risk assessment is not required for herbal medicinal products according to guidance CHMP/SWP/4447/00 Rev. 1 - Corr.

IV. CLINICAL ASPECTS

This is a national application submitted by Reckitt Benckiser Ireland Limited under Article 16c of Directive 2001/83/EC, as amended.

Strepsils Herbal Dry Cough Syrup is a traditional herbal medicinal product used for the symptomatic treatment of throat irritation and associated dry cough, 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 Strepsils Herbal Dry Cough Syrup 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 Strepsils Herbal Dry Cough Syrup 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.

The use of Strepsils Herbal Dry Cough Syrup should be avoided in those who are allergic to ribwort plantain and in those allergic to any of the other ingredients of this product.

The maximum dosage is 40ml per day; it is recommended that this dosage is not exceeded.

Strepsils Herbal Dry Cough Syrup is intended for oral short-term use only. It is recommended that if symptoms persist, worsen or do not improve after 7 days use of the product, a doctor or pharmacist should be consulted.

If dyspnoea, fever or purulent sputum occurs, it's recommended that a doctor be consulted.

Strepsils Herbal Dry Cough Syrup is not recommended for use in children under 12 years as safety data is lacking and medical advice should be sought.

As safety during pregnancy and breast-feeding has not been established, use during pregnancy and breast-feeding is not recommended.

Strepsils Herbal Dry Cough Syrup contains maltitol liquid (containing maltitol and sorbitol). This medicine contains up to 450 mg sorbitol in each 10 ml which is equivalent to 45 mg/ml. The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly. May have a mild laxative effect. Calorific value 2.3 kcal/g of maltitol liquid.

Patients with hereditary fructose intolerance (HFI), glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take or be given this medicinal product.

Strepsils Herbal Dry Cough Syrup contains 78.5 mg of alcohol (ethanol) in each 10 ml which is equivalent to 7.85 mg/ml (0.785% (w/v)). The amount in 10 ml of this medicine is equivalent to less than 2 ml beer or 1 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.

There are no known side effects associated with the active substance of Strepsils Herbal Dry Cough Syrup. Patients are advised to contact their doctor or pharmacist if side effects occur.

Overdose:
No case of overdose has 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 Strepsils Herbal Dry Cough Syrup.

The HPRA, on the basis of the data submitted, considered that Strepsils Herbal Dry Cough Syrup 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 Strepsils Herbal Dry Cough Syrup is granted.

VII. UPDATES

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
New Herbal	CRN00FN96	SmPC, IPAR and PIL		