IPAR

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

Medithyme Cough Syrup
Thyme herb liquid extract

TR0126/319/001
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 Medithyme cough syrup, containing a liquid extract of thyme herb.

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 Medithyme cough syrup. The active ingredient of Medithyme cough syrup is thyme herb liquid extract obtained from *Thymus vulgaris* L. herba (thyme herb).

II.1 S.1 Herbal Substance

The herbal substance is *Thymus vulgaris* L. herba (thyme herb), 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 thyme herb liquid 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 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.

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 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 Medithyme cough syrup.

III. NON-CLINICAL ASPECTS

The HPRA has been assured that good laboratory practice (GLP) standards were followed in an appropriate manner for the Ames test submitted to support the application.

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 the Ames test submitted no mutagenic effects were seen with a Thyme liquid extract of the same composition used in Medithyme Cough Syrup.

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

IV. CLINICAL ASPECTS

Medithyme Cough Syrup is a traditional herbal medicinal product used as an expectorant in productive cough associated with cold.
It is a traditional herbal medicinal product for use in the specified indication 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 Medithyme 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 Medithyme 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.

This traditional herbal medicinal product is for oral short-term use only.
If the symptoms persist, worsen or do not improve after one weeks use of Medithyme Cough Syrup, a qualified healthcare professional e.g. a doctor or pharmacist should be consulted.

This product is contraindicated in patients with hypersensitivity to thyme or to other members of the *Lamiaceae* (mint) family, or to any of the excipients listed in section 6.1 of the SmPC.

The use in children under 12 years of age is not recommended because medical advice should be sought.
The stated dose should not be exceeded.
When dyspnoea, fever or purulent sputum occurs, a doctor should be consulted.
This medicine contains 260 mg of alcohol (ethanol) in each dose (15 ml), which is equivalent to 2.2 % vol ethanol (alcohol). The amount in each dose (15 ml) of this medicine is equivalent to less than 7 ml beer or 3 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.

This medicine contains liquid maltitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine. Maltitol may have a mild laxative effect. Calorific value: 2.3 kcal/g maltitol.
This traditional herbal medicine contains 19.5 mg benzoate salt in each 15 ml dose.
This traditional herbal medicine contains less than 1 mmol sodium (23 mg) per 15 ml dose, that is to say essentially 'sodium-free'.

Patients who are treated with medicines known to interact with alcohol such as disulfiram or metronidazole should avoid this traditional herbal medicine because of the presence of ethanol in thyme liquid extract.
The concomitant use of multiple medicines that contain ethanol should be avoided.

Safety of the use of Medithyme Cough Syrup during pregnancy and lactation has not been established. In the absence of sufficient data, the use of Medithyme Cough Syrup during pregnancy and lactation is not recommended.

No studies on the effect on the ability to drive and use machines have been performed.
It should be kept in mind that Medithyme Cough Syrup contains 2.2% (v/v) alcohol.

Acute hypersensitivity reactions (including anaphylactoid reactions, such as oromucosal swelling, Quincke's oedema, dyspnoea, pruritus, rash and anaphylactic shock) have been reported in association with use of herbal medicinal products containing thyme, in some cases, in patients with a history of allergy/asthma.
Gastric disorders may occur. The frequency is not known.

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 Medithyme Cough Syrup.

The HPRA, on the basis of the data submitted, considered that Medithyme 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 Medithyme cough syrup is granted.

VI. REVISION DATE