IPAR

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

Buttercup Bronchostop Berry Flavour Cough Pastilles

Thyme herb dry extract

TR 2006/001/002

TR Holder: Kwizda Pharma GmbH

13 March 2015

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 Kwizda Pharma GmbH a Certificate of Traditional Use Registration for Buttercup Bronchostop Berry Flavour Cough Pastilles containing Thyme herb dry extract.

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 Buttercup Bronchostop Berry Flavour Cough Pastilles. The active ingredient of Buttercup Bronchostop Berry Flavour Cough Pastilles is a dry extract obtained from Thyme herb (*Thymus vulgaris* L. and *Thymus zygis* L., herba).
One pastille contains 59.5 mg of dry extract from *Thymus vulgaris* L. and *Thymus zygis* L., herba (Thyme herb) (DER 7-13:1) Extraction solvent: water.

II.1 S.1 Herbal Substance

The herbal substance specification is considered adequate to control the quality and meets current appropriate requirements.

II.2 S.2 Herbal preparation

The herbal preparation is Thyme herb dry extract. The herbal preparation 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 appropriate requirements.

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 suitably qualified manufacturing sites.

The manufacturing process is considered to be sufficiently validated.

P.4 Control of Other Substances

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 based on the pharmacopoeial monograph for Oromucosal Preparations. The tests and control limits are considered adequate for this type of product.

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 all packaging materials comply with EU legislation for use with foodstuffs 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 Buttercup Bronchostop Berry Flavour Cough Pastilles.

III NON-CLINICAL ASPECTS

Buttercup Bronchostop Berry Flavour Cough Pastilles 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. Given the type of application and limited data available, it is not possible to assess if the safety package for the phytochemical constituents of Buttercup Bronchostop Berry Flavour Cough Pastilles are acceptable to the standards of today's GLP and safety testing requirements.

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 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 Kwizda Pharma GmbH under Article 16c of Directive 2001/83/EC, as amended.
Buttercup Bronchostop Berry Flavour Cough Pastilles is a traditional herbal medicinal product used for the relief of coughs, such as chesty, dry, tickly, irritating coughs and catarrh 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 Buttercup Bronchostop Berry Flavour Cough Pastilles 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 Buttercup Bronchostop Berry Flavour Cough Pastilles 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.

For details on contraindications, warnings for use and possible side effects of please see the HPRA website for the SmPC for this THMP.

This THMP is indicated for short-term use only. Buttercup Bronchostop Berry Flavour Cough Pastilles are for oral use (allow to dissolve in the mouth through sucking).
This product is not recommended for use in children under 12 years of age
If symptoms worsen, or persist after 7 days, a doctor or a qualified Healthcare Professional e.g. a doctor or pharmacist should be consulted.

The only listed contraindication is:

Hypersensitivity to thyme or to other members of the *Lamiaceae* family, or to any of the excipients.

Regarding special warnings and precautions for use
If dyspnoea, fever or purulent sputum occurs, a doctor or qualified Healthcare Professional should be consulted.

This product is not recommended for use in children under 12 years of age
recommended due to lack of data.

Do not exceed the stated dose.

1 pastille corresponds to approximately 0.1 carbohydrate unit. This should be considered in patients with diabetes mellitus.

If symptoms worsen, or persist after 7 days, a doctor or qualified Healthcare Professional should be consulted.

In the absence of sufficient data, use during pregnancy and lactation is not recommended.

Regarding undesirable effects
Hypersensitivity reactions (including one case of anaphylactic shock and one case of
Quincke's edema) as well as stomach disorders have been observed in connection with medicinal products containing thyme. 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 Buttercup Bronchostop Berry Flavour Cough Pastilles.

The HPRA, on the basis of the data submitted, considered that Buttercup Bronchostop Berry Flavour Cough Pastilles demonstrated adequate evidence of traditional use for the approved indication(s) and no new preclinical or clinical safety concerns have been identified.

A Certificate of Traditional Use Registration for Buttercup Bronchostop Berry Flavour Cough Pastilles is granted.