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 IMB 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 IMB 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 Bio-Health Ltd a Certificate of Traditional Use Registration for Valdrian containing *Valeriana officinalis* L.

This application was submitted as a standard application according to Article 16.c of Directive 2001/83 EC, as amended as part of the Traditional Herbal Medicinal Product Registration Scheme.

About the product

The genus Valeriana belongs to the family Valerianaceae. The active ingredient of Valdrianis the powdered root of *Valeriana officinalis* L. The product is a clear hard capsule containing a light brown powder for oral use.

Valdrian is a traditional herbal medicinal product used for relief of symptoms of mild mental stressand to aid sleep, exclusively based on long-standing use.

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 Valdrian as a traditional herbal medicine and not upon data generated from clinical trials.

The Summary of Product Characteristics (SPC) and Patient Information Leaflet for this traditional herbal medicinal product are available on the HPRA website.

II. QUALITY ASPECTS

This application is for Valdrian hard capsules.

III.1.1 S.1 Herbal Substance

The herbal substance, powdered valerian root (*Valeriana officinalis* L. radix), is described in the European Pharmacopoeia and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP).

The herbal substance specification is considered adequate to control the quality and meets appropriate current requirements. The specification is supported by the batch analytical data provided.

III.1.3 Medicinal product

P.1 Composition

Hard capsule

The product is a clear capsule containing 400 mg powdered Valerian Root Ph. Eur. (light brown powder). The capsule shell is made of hypromellose.

P.2 Pharmaceutical Development

The product is an established pharmaceutical form and is manufactured according to a standard process.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The standard manufacturing process is adequately described and controlled.

P.4 Control of Other Substances (Excipients)

The hypromellose complies with Ph. Eur. requirements.

P.5 Control of Finished Product

The finished product specification is based on the pharmacopoeial monograph for capsules and the tests and control limits are considered appropriate for this type of product.

P.6 Packaging material

The product is presented in a HDPE plastic container with a HDPE tamper evident threaded-cap containing 60 capsules.

Evidence has been provided that the packaging materials comply with the legislation 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 demonstrating the stability of the product for 2 years when stored below 25°C.

III.1.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory pharmaceutical documentation has been provided, assuring consistent quality of Valdrian hard capsules.

III.1.5 Other information

Not applicable.

III.1.6 Conclusion on quality

The important quality characteristics of the product are defined and controlled. Satisfactory pharmaceutical documentation has been provided, assuring consistent quality of Valdrian hard capsules.

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 preclinical study has been submitted in relation to genotoxicity testing. This study was performed to GLP and indicated that Valdrian is not mutagenic.

Due to the nature of the application it is not possible to assess if the safety standards for the phytochemical constituents of Valdrian are acceptable to the standards of today's GLP and safety testing requirements. However, information presented demonstrating traditional use is acceptable and thus the lack of provision of a complete standard safety package is acceptable in compliance with guideline 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 Bio-Health Ltd to the Traditional Herbal Medicinal Products Registration Scheme, under Article 16c of Directive 2001/83 EC, as amended by Directive 2004/24 EC. The proposed indication is: A traditional herbal medicinal product for the relief of symptoms of mild mental stress and to aid sleep exclusively based on long-standing use.

III.3.1 Clinical Efficacy

No clinical efficacy data is required for registration of Traditional Herbal Medicinal Products (THMP). However, Article 16c1(c) 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. This traditional use data has been submitted and is satisfactory and is in accordance with Article 16c1(c).

The efficacy of this traditional herbal medicinal product is plausible on the basis of long standing use and experience.

The indication proposed for Valdrian is in line with traditional indications recorded and hence, compatible with the requirements of the Traditional Herbal Medicinal Products Directive 2004/24/EC.

III.3.2 Clinical Safety

In accordance with Article 16c1(d) the Applicant has provided a bibliographic review of the safety data together with an expert report.

Patients with known hypersensitivity to Valerian root should not use Valdrian.

Valdrian is recommended for oral short term use only.

This Traditional Herbal Medicinal Product is not recommended for children or adolescents under 18 years.

As a general precaution co-medication with hypnotics and other sedatives is not recommended as additive effects cannot be excluded. Valdrian may impair ability to drive and use machines. Patients who are affected should not drive or operate machinery.

The effect of Valdrian may be increased by alcohol. Excessive use of alcohol should therefore be avoided.

The safety of Valdrian during pregnancy and lactation has not been established, therefore, use during pregnancy and lactation is not recommended.

The possible side effects that may occur after ingesting Valdrian (valerian root) include gastrointestinal symptoms such as nausea and abdominal cramps. The frequency is not known.

Valerian root at a dose of approximately 20g (equivalent to 50 Valdrian capsules) is known to have caused symptoms such as fatigue, abdominal cramps, chest tightness, light headedness, hand tremor and dilation of the pupils which disappeared within 24 hours. If such symptoms arise, treatment should be supportive.

After intake of very high doses of Valerian root over several years (daily consumption corresponding to approximately 30g of the drug) withdrawal symptoms (delirium) have 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.

III.3.3 Pharmacovigilance

It should be noted that in accordance with Article 16g of Directive 2004/24, 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 Valdrian hard capsules.

The HPRA, on the basis of the data submitted, considered that Valdrian demonstrated adequate evidence of traditional use for the approved indications and no new preclinical or clinical safety concerns have been identified.

A certificate of traditional use for Valdrian is granted.

VI. REVISION DATE

April 2024

VII. UPDATES

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
MA Transfer	CRN00F6CY	SmPC section 7, 8, 10 Package Leaflet New MA Holder: HUK Europe Limited New PA number: TR25313/001/001	N/A	05/04/2024