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IRISH MEDICINES BOARD

PUBLIC ASSESSMENT REPORT FOR A TRADITIONAL HERBAL MEDICINAL PRODUCT FOR HUMAN USE

Holland & Barrett Valerian Hard Capsules
Valerian root dry extract

TR 1563/1/1
TR holder NBTY Europe Ltd T/A Holland and Barrett Limited

Date 1st of February 2013

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 Irish Medicines Board (IMB) 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 IMB 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 IMB has granted NBTY Europe Ltd a Certificate of Traditional Use Registration for Holland & Barrett Valerian hard capsules, containing dry extract from valerian root (*Valeriana officinalis* L.).

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 IMB's website.

II QUALITY ASPECTS

This application is for Holland & Barrett Valerian hard capsules. The active ingredient of Holland & Barrett Valerian hard capsules is an extract obtained from valerian root (*Valeriana officinalis* L.).

Each hard capsule contains 337 mg of extract (as dry extract) from valerian root (*Valeriana officinalis* L.) (equivalent to 1683 mg-2020 mg of valerian root). Extraction solvent: ethanol 70% v/v.

II.1 S.1 Herbal Substance

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

II.2 S.2 Herbal preparation

The herbal preparation is dry extract from Valerian root (*Valeriana officinalis* L.) and is manufactured in accordance with the principles of good manufacturing practice (GMP)

The herbal preparation specification is considered adequate to control the quality. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

The capsules are two piece and clear with a grey/brown fill.

Each capsule contains 337 mg of extract (as dry extract) from valerian root (*Valeriana officinalis* L.) (equivalent to 1683 mg-2020 mg of valerian root). Extraction solvent: ethanol 70% v/v.
Each capsule also contains the following inactive ingredients: magnesium stearate, maltodextrin and silica colloidal anhydrous. The capsule shell is made from hypromellose.

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 good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process is standard and is considered valid.

P.4 Control of Other Substances (Excipients)

All ingredients comply with Ph. Eur.

P.5 Control of Finished Product

The Finished Product Specification, the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described and are supported by validation data, as appropriate.

Batch analytical data have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The product is presented in green polyethylene terephthalate (PET) bottles with a polypropylene cap and an inner seal. Pack sizes of 30 or 60 capsules are available.

Evidence has been provided that packaging complies with EU legislation requirements 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^{o}C, protected from light and moisture.

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 Holland & Barrett Valerian Hard Capsules.

III NON-CLINICAL ASPECTS

Holland & Barrett Valerian Hard capsules is a traditional herbal medicinal product as defined by Article 16a(1) of Directive 2001/83/EC as amended. Given the type of application and limited data available, it is not possible to assess if the safety standards for the phytochemical constituents of Valerian root extract are acceptable to the standards of today’s GLP and safety testing requirements.

While no new preclinical studies have been submitted, an expert report on safety has been provided which includes a review of the available literature. Appropriate testing for genotoxicity, carcinogenicity and reproductive toxicity has not been performed, however a discussion regarding these individual areas has been provided with respect to the current available literature data. In view of the absence of genotoxicity data the applicant is required to submit this data within two years of the granting of a certificate of registration.

Overall, the information presented demonstrating traditional use is acceptable and thus the lack of provision of a complete standard safety package is acceptable and 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 NBTY Europe Ltd under Article 16a of Directive 2001/83/EC, as amended.

Holland & Barrett Valerian Hard capsules is a traditional herbal medicinal product used for the relief of symptoms of mild mental stress and to aid sleep, 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 Nature's Bounty Valerian Hard capsules 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 Holland & Barrett Valerian Hard capsules 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 maximum dosage is 4 capsules per day; it is recommended that this dosage is not exceeded.

The use of Holland & Barrett Valerian Hard capsules should be avoided in those who are allergic to Valerian and in those allergic to any of the other ingredients of this product.

Holland & Barrett Valerian Hard capsules are intended for oral short-term use only. It is recommended that if symptoms persist, worsen or do not improve after 2 weeks use of the product, a doctor or pharmacist should be consulted.

Holland & Barrett Valerian Hard capsules is not recommended for use in children and adolescents under 18 years as safety data is lacking and medical advice should be sought.

The effects of this product may be increased by alcohol and other medicines which can cause drowsiness.

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

Holland & BarrettValerian Hard capsules may cause drowsiness. If affected, patients should not drive or operate machinery.

The possible side effects that may occur after ingesting Holland & Barrett Valerian Hard capsules include stomach cramps and nausea. Patients are advised to contact their doctor or pharmacist if side effects become troublesome or other side effects occur.

After intake of very high doses of Valerian root over several years withdrawal symptoms 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.

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 Holland & Barrett Valerian Hard Capsules.

The IMB, on the basis of the data submitted, considers that Holland & Barrett Valerian hard capsules 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 registration for Holland & Barrett Valerian Hard capsules is granted.