IPAR

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

Natures Aid Sleepeeze Valerian Tablets
Valerian root extract

TR0126/316/001
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 Natures Aid Sleepeeze Valerian tablets, containing a dry extract of valerian root.

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 Natures Aid Sleepeeze Valerian tablets. The active ingredient of Natures Aid Sleepeeze Valerian tablets is a dry extract obtained from *Valeriana officinalis* L., radix (Valerian root).

II.1 S.1 Herbal Substance

The herbal substance is *Valeriana officinalis* L., radix (Valerian root) 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 Valerian dry hydroalcoholic extract, described in the European Pharmacopoeia, 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 is considered to be sufficiently validated.

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

All ingredients comply with Ph. Eur., with the exception of the film coat, which is 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 tablets, 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 Natures Aid Sleepeeze Valerian tablets.

III. NON-CLINICAL ASPECTS

Natures Aid Sleepeeze Valerian Tablets 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 Natures Aid Sleepeeze Valerian Tablets 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).

A GLP compliant Ames test has been submitted which did not reveal a risk of mutagenicity associated with Natures Aid Sleepeeze Valerian Tablets. Carcinogenicity and reproductive toxicity testing has not been conducted.

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 Clonmel Healthcare Limited under Article 16c of Directive 2001/83/EC, as amended.

Natures Aid Sleepeeze Valerian Tablets is a traditional herbal medicinal product used for the relief of mild symptoms of mental stress and to aid sleep 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 Natures Aid Sleepeeze Valerian Tablets 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 Natures Aid Sleepeeze Valerian Tablets 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 Natures Aid Sleepeeze Valerian Tablets should be avoided in those who are allergic to Valerian and in those allergic to any of the other ingredients of this product.

The maximum dosage is 3 tablets per day; it is recommended that this dosage is not exceeded.

Natures Aid Sleepeeze Valerian Tablets 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.

Natures Aid Sleepeeze Valerian Tablets are not recommended for use in children and adolescents under 18 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.

Natures Aid Sleepeeze Valerian Tablets may cause drowsiness. If affected, patients should not drive or operate machinery.

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

Each tablet contains glucose 2.4 mg. Patients with rare glucose-galactose malabsorption should not take this medicine.

The possible side effects that may occur after ingesting Natures Aid Sleepeeze Valerian Tablets include stomach cramps and nausea. Patients are advised to contact their doctor or pharmacist if side effects become troublesome or other side effects occur.

Overdose:

Valerian root at a dose of approximately 20 g (equivalent to 22-27 Sleepeeze Valerian Tablets) caused benign symptoms (fatigue, abdominal cramp, chest tightness, lightheadedness, hand tremor and dilation of the pupils), which disappeared within

24 hours. If symptoms arise, treatment should be supportive. After intake of very high doses of valerian root over several years (daily consumption corresponding to approximately 10 g 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.

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 Natures Aid Sleepeeze Valerian tablets.

The HPRA, on the basis of the data submitted, considered that Natures Aid Sleepeeze Valerian tablets 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 Natures Aid Sleepeeze Valerian tablets is granted.

VI. REVISION DATE

25/08/2027

VII. UPDATES