LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Läkemedelsverket 2014-10-16

Public Assessment Report
Scientific discussion

Dormeasan, oral drops, solution
(*Valeriana officinalis* L., radix, tincture; *Humulus lupulus* L., strobulus, tincture)

Asp. No: 2008-1029

This module reflects the scientific discussion for the approval of Dormeasan, oral drops, solution. The procedure was finalised at 2011-09-30. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se

LAY SUMMARY

The Medical Products Agency (Läkemedelsverket, MPA) has granted Svenska Bioforce AB, a traditional-use registration for the herbal medicinal product Dormeasan, oral drops, solution. This product is available without prescription and can be bought from pharmacies and other outlets.

Dormeasan is traditionally used for temporary insomnia and minor nervous tension. The active ingredients are tinctures of *Valeriana officinalis* L., radix (vänderot) and *Humulus lupulus* L., strobulus (humle). This registration is based exclusively upon evidence of traditional use of the fixed combination of *Valeriana officinalis* and *Humulus lupulus* as a herbal medicinal product and not upon data generated from clinical trials. For traditional herbal medicinal products there is no requirement to scientifically prove the effect; adequate evidence of traditional use is sufficient.

The chemical/pharmaceutical quality of the product is acceptable and no new or unexpected safety concerns have been identified during the assessment. It was therefore decided that Dormeasan could be registered as a traditional herbal medicinal product.

I. INTRODUCTION

Svenska Bioforce AB has applied for a traditional-use registration for Dormeasan, oral drops, solution. The application was submitted under Article 16a traditional use registration for herbal medicinal products of the Directive 2001/83 EC, as amended. The application is a national application for Sweden.

The active substances are *Valeriana officinalis* L., radix, tincture and *Humulus lupulus* L., strobulus, tincture.
For approved indications, see the Summary of Product Characteristics.

Dormeasan, oral drops, solution was first authorised as a natural remedy in 1997-01-09. As a consequence of the new legislation regarding (traditional) herbal medicinal products the product was reclassified as a traditional herbal medicinal product in 2011-09-30.

II. QUALITY ASPECTS

II.1 Introduction

Dormeasan is presented in the form of oral drops, solution containing 460 mg tincture of the active substance *Valeriana officinalis* L., radix, which corresponds to approximately 240 mg of fresh root of valerian, and 460 mg tincture of the active substance *Humulus lupulus* L., strobulus, which corresponds to approximately 230 mg fresh female inflorescence of hop.

No excipients are added apart from the extraction solvents.

All manufacturers involved in the production operate in accordance with EU-GMP, or where relevant, GACP (Good Manufacturing Practise and Good Agricultural and Collection Practice, respectively).

II.2 Drug Substance

The herbal substances are *Valeriana officinalis* L., radix and *Humulus lupulus* L., strobulus. The Swedish names are “vänderot” and “humle”, respectively.

The plants used are cultivated in Central Europe (Switzerland and Germany). Relevant information on growing conditions and controls of the herbal substance (such as residues of heavy metals and pesticides as well as microbiological quality) has been provided.

The fresh herbal substances are cut and macerated with ethanol separately. At the end of the maceration time, the macerates are pressed off using high pressure. The resulting raw tinctures are then clarified by sedimentation.

The manufacturing process has been adequately described and satisfactory specifications have been provided for starting materials (herbal substance) and excipients/solvents. The tests and limits in the specifications are considered appropriate to control the quality in relation to the intended purpose.

The active substances are tinctures of *Valeriana officinalis* L., radix and *Humulus lupulus* L., strobulus. The active substance (herbal preparation) specification includes relevant tests and the limits for impurities have been justified. The analytical methods applied are suitably described and validated.

II.3 Medicinal Product

Dormeasan, oral drops, solution is formulated without any excipients apart from the extraction solvent, which are described in the current European Pharmacopoeia. All raw materials used in the product are safe with view to possible TSE/BSE risk.

The manufacturing process has been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control and ensure both batch to batch reproducibility and compliance with the product specification.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies under ICH conditions have been performed and data presented support the shelf life claimed in the SmPC.

III. NON-CLINICAL AND CLINICAL ASPECTS

III.1 Introduction

The safety and traditional use of *Valeriana officinalis* L., radix and *Humulus lupulus* L., flos have been evaluated by the Committee on Herbal Medicinal Products (HMPC) and has issued a Community monograph on the fixed combination. The product characteristic of Dormeasan is in agreement with the one described in the HMPC monograph.
The reader is referred to the Community monograph and the pertinent assessment reports for details.

III.2 Non-clinical aspects

The applicant has collected available information from the literature in the areas of non-clinical pharmacology and toxicology. This information has been assessed by the MPA and no signals of non-clinical safety concern have been identified. The exact mechanism of action of *Valeriana officinalis* L., radix, tincture and *Humulus lupulus* L., strobulus, tincture in relation to its traditional medicinal use cannot be considered clarified.

A product/extract specific study on mutagenic activity has been performed. The extract has been shown not to be mutagenic in Ames test.

Based on the non-clinical information, both from the literature and the product specific study, no objections are raised to the approval of *Valeriana officinalis* L., radix, tincture and *Humulus lupulus* L., strobulus, tincture as active ingredients in a traditional herbal medicinal product.

III.3 Ecotoxicity/environmental risk assessment

Dormeasan is a traditional herbal medicinal product. According to “Guideline on the environmental risk assessment of medicinal products for human use”

(EMEA/CHMP/SWP/4447/00), (traditional) herbal medicinal products are exempted from the obligation to present an environmental risk assessment due to the nature of their constituents.

III.4 Clinical aspects

Results of clinical trials concerning clinical efficacy and safety are not required for the registration of a traditional herbal medicinal product.

III.5 Traditional use

The applicant has provided a bibliographic review, which shows sufficient evidence for the medicinal use of *Valeriana officinalis,* radix and *Humulus lupulus,* strobulus throughout a period of at least 30 years, including at least 15 years within the Community

The product itself has been registered as a traditional herbal medicinal product, under the Article 16a of the Directive 2001/83 EC as amended.

III.6 Clinical safety

Longstanding medicinal use and experience of *Valeriana officinalis,* radix and *Humulus lupulus,* strobulus, has been documented. During this time, no clinical signals that *Valeriana officinalis,* radix and *Humulus lupulus,* strobulus is harmful under normal conditions of use have been identified. A periodic safety update report (PSUR) for the product Dormeasan, oral drops, solution supports this statement.

As no data on use in children are available, products containing *Valeriana officinalis,* radix and *Humulus lupulus,* strobulus *cannot* be recommended for use in children below the age of 12 years.

Due to lack of safety data, the use of products containing *Valeriana officinalis,* radix and *Humulus lupulus,* strobulus during pregnancy and lactation is not recommended.

Based on the clinical safety information available, no objections are raised to the approval of Dormeasan as a traditional herbal medicinal product.

IV. PRODUCT INFORMATION

The product information (Summary of Product Characteristics, Package Leaflet and labelling) has been assessed and accepted by the Medical Products Agency.

V. OVERALL CONCLUSION, RISK ASSESSMENT AND RECOMMENDATION

For Dormeasan, the handling, manufacture and quality control of raw materials, active substance and finished product are in line with GMP and pharmacopoeial requirements. The applicant has shown that the chemical/pharmaceutical quality is acceptable and can confirm that the process is under control and ensures both batch reproducibility and compliance with the product specification.

The applicant has provided evidence that the tinctures in Dormeasan has had a medicinal use for at least 30 years, including at least 15 years within the Community.

No signals of preclinical or clinical safety concern have been identified under normal conditions of use.

Dormeasan, oral drops, solution, can be recommended for registration as a traditional herbal medicinal product.

VI. APPROVAL

Dormeasan, oral drops, solution was approved in the national procedure on 2011-09-30.

Public Assessment Report – Update

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
5.4.3-2016-16399	Declaration of active substance – Corresponding quantities of herbal drugs corrected.	SmPC, PIL,. Labelling	2016-11-09	Approval	N/A

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se