Sedorma tablets

THR 16672/0023

UKPAR

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LAY SUMMARY

Sedorma tablets

THR 16627/0023

The Medicines and Healthcare products Regulatory Agency (MHRA) granted WEBER & WEBER GMBH & Co. KG a Traditional Herbal Registration certificate for the traditional herbal medicinal product Sedorma tablets (Traditional Herbal Registration number: THR 16627/0023) on 06 March 2019. Sedorma tablets are available without prescription and can be obtained from pharmacies and non-pharmacy outlets.

Each coated tablet of Sedorma contains the active substances:

- 67.5 mg of extract (as dry extract) from Lavender flower (*Lavandula angustifolia* Miller) (4-8:1), extraction solvent ethanol 70% v/v
- 37.5 mg of extract (as dry extract) from Hop strobile (*Humulus lupulus* L.) (3-7:1), extraction solvent ethanol 50% v/v
- 75 mg of extract (as dry extract) from Lemon balm leaf (*Melissa officinalis* L.) (4-8:1), extraction solvent ethanol 50% v/v
- 112.5 mg of extract (as dry extract) from Passion flower herb (*Passiflora incarnata* L.) (3-6:1), extraction solvent ethanol 50% v/v
- 100 mg of extract (as dry extract) from Valerian root (*Valeriana officinalis* L.) (3-6:1), extraction solvent ethanol 70% v/v

Sedorma tablets is a traditional herbal medicinal product used for the temporary relief of symptoms associated with stress such as mild anxiety and to aid sleep, based on traditional use only. This registration is based exclusively upon the longstanding use of Lavender flower, Hop strobile, Lemon balm leaf, Passion flower herb and Valerian root as a traditional herbal medicine and not upon data generated from clinical trials. There is no requirement under the Traditional Herbal Registration Scheme to prove scientifically that a product works.

No new or unexpected safety concerns arose from this application and it was, therefore, decided that a Traditional Herbal Registration Certificate could be granted.
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INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted WEBER & WEBER GMBH & Co. KG a Traditional Herbal Registration certificate for the traditional herbal medicinal product Sedorma tablets (Traditional Herbal Registration number: THR 16672/0023) on 06 March 2019. Sedorma tablets are available without prescription and can be obtained from pharmacies and non-pharmacy outlets.

The application was submitted according to Article 16.c of Directive 2001/83 EC, as amended, as part of the Traditional Herbal Medicines Registration Scheme. Sedorma tablets is a traditional herbal medicinal product used for the temporary relief of symptoms associated with stress such as mild anxiety and to aid sleep, based on traditional use only.

The data supplied by the applicant demonstrates 30 years of traditional use of Lavender flower, Hop strobile, Lemon balm leaf, Passion flower herb and Valerian root in the European Union. A satisfactory review of the available safety data on Lavender flower, Hop strobile, Lemon balm leaf, Passion flower herb and Valerian root has also been provided, together with an Expert Safety Report supporting the proposed product.
HERBAL SUBSTANCE: LAVENDER FLOWER
Latin name of the plant: Lavandula angustifolia Mill.
Common name of the plant: Lavender
Plant family: Lamiaceae

Manufacture of Herbal Substance
The herbal substance consists of dried lavender flowers.
Confirmation has been provided that the herbal substance is produced in line with the Good Agricultural and Collection Practice (GACP) guideline and that the herbal substance has not been fumigated or treated with ionizing radiation.

Control of Herbal Substance
An appropriate specification based on the Ph Eur monograph is applied and is acceptable. The specification is supported by the batch data provided.

Container Closure System
Satisfactory details of the container closure system are provided and confirmation has been given that all components of the container closure system comply with current legislation relating to plastic materials and articles intended to come into contact with foodstuffs.

Stability of Herbal Substance
Confirmation is given that the herbal substance will be tested prior to being used to make the herbal preparation. A shelf-life for the herbal substance is not necessary because it is only a precursor of the active substance, the herbal preparation. The guideline requires stability testing data for the herbal preparation and the herbal product in the application documents and not for the herbal substance.

HERBAL PREPARATION: LAVENDER FLOWER DRY EXTRACT

Ratio of the herbal substance to the herbal preparation (native): 4-8:1
Extraction solvent: Ethanol 70% v/v

Manufacture
A satisfactory description of the manufacturing process of the herbal preparation has been provided. The in-process controls are satisfactorily detailed.

There are no critical steps identified as the manufacture of the herbal preparation is considered a standard procedure.

Certificates of analysis for all materials used in the manufacture of the herbal preparation have been provided.

Control of Herbal Preparation
A satisfactory specification with appropriate tests and limits has been provided for the herbal preparation.

Satisfactory analytical procedures are used to control the quality of the herbal preparation. Analytical procedures have been validated, as appropriate.
Certificates of analysis have been provided for production batches of the herbal preparation, demonstrating satisfactory compliance with the proposed specification.

**Container Closure System**
Confirmation is provided that all components of the container closure system used to store the herbal preparation comply with Directive 2008/39/EC relating to plastic materials and articles intended to come into contact with foodstuffs.

**Stability**
Stability studies have been performed in accordance with current guidelines. The proposed re-test period for the herbal preparation is acceptable.

**HERBAL SUBSTANCE:** HOP STROBILE

<table>
<thead>
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<th>Latin name of the plant:</th>
<th>Humulus lupulus L.</th>
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<td>Common name of the plant:</td>
<td>Hop/Hops</td>
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<td>Plant family:</td>
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**Manufacture of Herbal Substance**
The herbal substance is dried, generally whole, female inflorescence of Hop strobile.

Confirmation has been provided that the herbal substance is produced in line with the Good Agricultural and Collection Practice (GACP) guideline and that the herbal substance has not been fumigated or treated with ionizing radiation.

**Control of Herbal Substance**
An appropriate specification based on the Ph Eur monograph is applied and is acceptable. The specification is supported by the batch data provided.

**Container Closure System**
Satisfactory details of the container closure system are provided and confirmation has been given that all components of the container closure system comply with current legislation relating to plastic materials and articles intended to come into contact with foodstuffs.

**Stability of Herbal Substance**
Confirmation is given that the herbal substance will be tested prior to being used to make the herbal preparation. A shelf-life for the herbal substance is not necessary because it is only a precursor of the active substance, the herbal preparation. The guideline requires stability testing data for the herbal preparation and the herbal product in the application documents and not for the herbal substance.

**HERBAL PREPARATION:** HOP STROBILE DRY EXTRACT

| Ratio of the herbal substance to the herbal preparation (native): | 3-7:1 |
| Extraction solvent: | Ethanol 50% v/v |

**Manufacture**
A satisfactory description of the manufacturing process of the herbal preparation has been provided. The in-process controls are satisfactorily detailed.

There are no critical steps identified as the manufacture of the herbal preparation is considered a
standard procedure.

Certificates of analysis for all materials used in the manufacture of the herbal preparation have been provided.

**Control of Herbal Preparation**
A satisfactory specification with appropriate tests and limits has been provided for the herbal preparation.

Satisfactory analytical procedures are used to control the quality of the herbal preparation. Analytical procedures have been validated, as appropriate.

Certificates of analysis have been provided for production batches of the herbal preparation, demonstrating satisfactory compliance with the proposed specification.

**Container Closure System**
Confirmation is provided that all components of the container closure system used to store the herbal preparation comply with Directive 2008/39/EC relating to plastic materials and articles intended to come into contact with foodstuffs.

**Stability**
Stability studies have been performed in accordance with current guidelines. The proposed re-test period for the herbal preparation is acceptable.

**HERBAL SUBSTANCE:** LEMON BALM LEAF
**Latin name of the plant:** Melissa officinalis L.
**Common name of the plant:** Melissa
**Plant family:** Lamiaceae

**Manufacture of Herbal Substance**
The herbal substance is dried Lemon balm leaf.
Confirmation has been provided that the herbal substance is produced in line with the Good Agricultural and Collection Practice (GACP) guideline and that the herbal substance has not been fumigated or treated with ionizing radiation.

**Control of Herbal Substance**
An appropriate specification based on the Ph Eur monograph is applied and is acceptable. The specification is supported by the batch data provided.

**Container Closure System**
Satisfactory details of the container closure system are provided and confirmation has been given that all components of the container closure system comply with current legislation relating to plastic materials and articles intended to come into contact with foodstuffs.

**Stability of Herbal Substance**
Confirmation is given that the herbal substance will be tested prior to being used to make the herbal preparation. A shelf-life for the herbal substance is not necessary because it is only a precursor of the active substance, the herbal preparation. The guideline requires stability testing data for the herbal preparation and the herbal product in the application documents and not for the herbal substance.
HERBAL PREPARATION: MELISSA LEAF DRY EXTRACT

Ratio of the herbal substance to the herbal preparation (native): 4-8:1
Extraction solvent: Ethanol 50% v/v

Manufacture
A satisfactory description of the manufacturing process of the herbal preparation has been provided. The in-process controls are satisfactorily detailed.

There are no critical steps identified as the manufacture of the herbal preparation is considered a standard procedure.

Certificates of analysis for all materials used in the manufacture of the herbal preparation have been provided.

Control of Herbal Preparation
A satisfactory specification with appropriate tests and limits has been provided for the herbal preparation.

Satisfactory analytical procedures are used to control the quality of the herbal preparation. Analytical procedures have been validated, as appropriate.

Certificates of analysis have been provided for production batches of the herbal preparation, demonstrating satisfactory compliance with the proposed specification.

Container Closure System
Confirmation is provided that all components of the container closure system used to store the herbal preparation comply with Directive 2008/39/EC relating to plastic materials and articles intended to come into contact with foodstuffs.

Stability
Stability studies have been performed in accordance with current guidelines. The proposed re-test period for the herbal preparation is acceptable.

HERBAL SUBSTANCE: PASSION FLOWER HERB

Latin name of the plant: Passiflora incarnata L.
Common name of the plant: Passion flower
Plant family: Passifloraceae

Manufacture of Herbal Substance
The herbal substance is the fragmented or cut, dried aerial parts of Passion flower. It may also contain flowers and/or fruits.

Confirmation has been provided that the herbal substance is produced in line with the Good Agricultural and Collection Practice (GACP) guideline and that the herbal substance has not been fumigated or treated with ionizing radiation.

Control of Herbal Substance
An appropriate specification based on the Ph Eur monograph is applied and is acceptable. The
specification is supported by the batch data provided.

**Container Closure System**

Satisfactory details of the container closure system are provided and confirmation has been given that all components of the container closure system comply with current legislation relating to plastic materials and articles intended to come into contact with foodstuffs.

**Stability of Herbal Substance**

Confirmation is given that the herbal substance will be tested prior to being used to make the herbal preparation. A shelf-life for the herbal substance is not necessary because it is only a precursor of the active substance, the herbal preparation. The guideline requires stability testing data for the herbal preparation and the herbal product in the application documents and not for the herbal substance.

**HERBAL PREPARATION:**

**PASSION FLOWER DRY EXTRACT**

| Ratio of the herbal substance to the herbal preparation (native): | 3-6:1 |
| Extraction solvent: | Ethanol 50% v/v |

**Manufacture**

A satisfactory description of the manufacturing process of the herbal preparation has been provided. The in-process controls are satisfactorily detailed.

There are no critical steps identified as the manufacture of the herbal preparation is considered a standard procedure.

Certificates of analysis for all materials used in the manufacture of the herbal preparation have been provided.

**Control of Herbal Preparation**

A satisfactory specification with appropriate tests and limits has been provided for the herbal preparation.

Satisfactory analytical procedures are used to control the quality of the herbal preparation. Analytical procedures have been validated, as appropriate.

Certificates of analysis have been provided for production batches of the herbal preparation, demonstrating satisfactory compliance with the proposed specification.

**Container Closure System**

Confirmation is provided that all components of the container closure system used to store the herbal preparation comply with Directive 2008/39/EC relating to plastic materials and articles intended to come into contact with foodstuffs.

**Stability**

Stability studies have been performed in accordance with current guidelines. The proposed re-test period for the herbal preparation is acceptable.

**HERBAL SUBSTANCE:**

**VALERIAN ROOT**

| Latin name of the plant: | Valeriana officinalis L. |
| Common name of the plant: | Valerian |
Plant family: Valerianaceae

Manufacture of Herbal Substance
The herbal substance is the dried, whole or fragmented underground parts of Valerian root, including the rhizome surrounded by the roots and stolons.

Confirmation has been provided that the herbal substance is produced in line with the Good Agricultural and Collection Practice (GACP) guideline and that the herbal substance has not been fumigated or treated with ionizing radiation.

Control of Herbal Substance
An appropriate specification based on the Ph Eur monograph is applied and is acceptable. The specification is supported by the batch data provided.

Container Closure System
Satisfactory details of the container closure system are provided and confirmation has been given that all components of the container closure system comply with current legislation relating to plastic materials and articles intended to come into contact with foodstuffs.

Stability of Herbal Substance
Confirmation is given that the herbal substance will be tested prior to being used to make the herbal preparation. A shelf-life for the herbal substance is not necessary because it is only a precursor of the active substance, the herbal preparation. The guideline requires stability testing data for the herbal preparation and the herbal product in the application documents and not for the herbal substance.

**HERBAL PREPARATION:** VALERIAN ROOT DRY EXTRACT

| Ratio of the herbal substance to the herbal preparation (native): | 3-6:1 |
| Extraction solvent: | Ethanol 70% v/v |

Manufacture
A satisfactory description of the manufacturing process of the herbal preparation has been provided. The in-process controls are satisfactorily detailed.

There are no critical steps identified as the manufacture of the herbal preparation is considered a standard procedure.

Certificates of analysis for all materials used in the manufacture of the herbal preparation have been provided.

Control of Herbal Preparation
A satisfactory specification with appropriate tests and limits has been provided for the herbal preparation.

Satisfactory analytical procedures are used to control the quality of the herbal preparation. Analytical procedures have been validated, as appropriate.

Certificates of analysis have been provided for production batches of the herbal preparation, demonstrating satisfactory compliance with the proposed specification.

Container Closure System
Confirmation is provided that all components of the container closure system used to store the herbal preparation comply with Directive 2008/39/EC relating to plastic materials and articles intended to come into contact with foodstuffs.

**Stability**

Stability studies have been performed in accordance with current guidelines. The proposed re-test period for the herbal preparation is acceptable.

**HERBAL PRODUCT: SEDORMA TABLETS**

**Description and Composition of Herbal Product**

Sedorma tablets are light green, round, biconvex, shiny sugar-coated tablets.

Each coated tablet contains the active substances:

- 67.5 mg of extract (as dry extract) from Lavender flower (*Lavandula angustifolia* Miller) (4-8:1), extraction solvent ethanol 70% v/v
- 37.5 mg of extract (as dry extract) from Hop strobile (*Humulus lupulus* L.) (3-7:1), extraction solvent ethanol 50% v/v
- 75 mg of extract (as dry extract) from Lemon balm leaf (*Melissa officinalis* L.) (4-8:1), extraction solvent ethanol 50% v/v
- 112.5 mg of extract (as dry extract) from Passion flower herb (*Passiflora incarnata* L.) (3-6:1), extraction solvent ethanol 50% v/v
- 100 mg of extract (as dry extract) from Valerian root (*Valeriana officinalis* L.) (3-6:1), extraction solvent ethanol 70% v/v

Each coated tablet contains 6.1 mg of glucose and 220.3 mg of sucrose (see Section 4.4. `Special warnings and precautions for use` of the SmPC).

Other excipients include extract excipients which consist of maltodextrin, and silica, colloidal anhydrous. The tablet core consists of the excipients cellulose, croscarmellose sodium, silica, colloidal anhydrous, talc and stearic acid. The tablet coating consists of sucrose, talc, shellac, titanium dioxide, acacia, calcium carbonate, tragacanth, glucose, riboflavin, brilliant blue beeswax, white Carnauba wax.

The compatibility of the herbal preparations with the excipients is demonstrated by the stability testing results. The excipients are controlled in line with their respective Ph Eur monograph.

None of the excipients used contain material of animal or human origin. This product does not contain or consist of genetically modified organisms (GMO).

**Manufacture of Herbal Product**

A satisfactory description of the manufacturing process and in-process controls are provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on commercial batches and the results are satisfactory.

**Control of Herbal Product**

A satisfactory finished product specification with appropriate tests and limits has been provided.
Acceptance limits have been justified with respect to conventional pharmaceutical requirements, and where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification.

**Container Closure System**
Sedorma tablets are provided in PVC/PVDC-aluminium blister packs containing 10, 20 or 60 tablets inserted into a carton. Not all pack sizes may be marketed.

Suitable specifications have been provided by the packaging suppliers and it has been confirmed that all primary packaging materials comply with current regulations.

**Stability of Herbal Product**
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a product shelf-life of 3 years is appropriate when the storage precautions ‘Do not store above 25° C’ and ‘Store in the original package’ are applied.

**Pharmaceutical Expert**
The Quality Overall Summary has been written by an expert with suitable experience.

**Product Literature**
All product literature is satisfactory.

A package leaflet has been submitted to the MHRA along with results of a consultation with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

**CONCLUSION**
There are no objections to granting of a Traditional Herbal Registration from a quality point of view.

**NON-CLINICAL ASSESSMENT**

**NON-CLINICAL OVERVIEW**
The applicant has submitted a literature review with this application. An Expert Safety Report was provided, which included reviews of some non-clinical data. The Expert Safety Report was written by a suitably qualified professional.

The overview submitted in support of this application is satisfactory.

The applicant has provided assurance that the results of appropriate genotoxicity testing will be submitted prior to the first renewal of the registration

**SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)**
The SmPC for this product is satisfactory from a non-clinical point of view.

**ENVIRONMENTAL RISK ASSESSMENT**
An environmental risk assessment is not required for herbal medicinal products according to guidance CHMP/SWP/4447/00.
CONCLUSION
There are no objections to granting of a Traditional Herbal Registration from a non-clinical point of view.

CLINICAL ASSESSMENT

INDICATIONS
The applicant submitted the following therapeutic indication for Sedorma tablets (THR 16672/0023):

“Sedorma is a traditional herbal medicinal product used for the temporary relief of symptoms associated with stress such as mild anxiety and to aid sleep, based on traditional use only.”
This is acceptable.

POSOLOGY AND METHOD OF ADMINISTRATION

For adults and the elderly
1 tablet twice a day with some water.

The use in children and adolescents under 18 years of age is not recommended (see section 4.4 `Special warnings and precautions for use`).

Duration of use:
For short term use only.

If the symptoms worsen, or persist longer than 2 weeks during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

EFFICACY
No clinical efficacy data are required for the registration of Traditional Herbal Medicinal Products.

EVIDENCE OF TRADITIONAL USE
Article 16 c 1 (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 EU.

The applicant has provided a bibliographic review as evidence of the use of the combination of extracts of Lavender flower, Hop strobile, Lemon balm leaf, Passion flower herb and Valerian root within the EU for a period exceeding 30 years. Additionally, the HMPC Assessment Reports and European herbal monographs cover the evidence for the traditional use of these extracts in the EU for at least 30 years. The information provided is considered to satisfy the requirement to demonstrate use for at least 30 years of which at least 15 years have been in an EU Member State. The requirements of the Directive are therefore addressed for this aspect.

SAFETY REVIEW
Article 16 c 1 (d) requires the applicant to provide a bibliographic review of the safety data together with an Expert Safety Report.

A safety review has been provided as well as an Expert Safety Report written by a suitably qualified professional. In addition the HMPC Assessment Reports for extracts of Lavender flower, Hop strobile, Lemon balm leaf, Passion flower herb and Valerian root cover the bibliographic safety data available.
**PRODUCT LITERATURE**
The SmPC, PIL and labelling for this product is medically satisfactory.

**CONCLUSION**
There are no objections to granting of a Traditional Herbal Registration from a clinical point of view.

**OVERALL CONCLUSION AND RISK ASSESSMENT**

**QUALITY**
The quality data submitted with this application are satisfactory.

**NON-CLINICAL**
New non-clinical data are generally not required for an application of this type. Genotoxicity data has not been submitted and an assurance has been provided that appropriate genotoxicity testing will be carried out prior to the first renewal of the registration.

**Efficacy and Safety**
No clinical efficacy data are required for registration of Traditional Herbal Medicinal Products. The applicant has provided a bibliographic review which shows sufficient evidence for the use of the combination of extracts of Lavender flower, Hop strobile, Lemon balm leaf, Passion flower herb and Valerian root within the EU for a period exceeding 30 years.

The published HMPC Assessment Reports and European herbal monographs for Lavender flower, Hop strobile, Lemon balm leaf, Passion flower herb and Valerian root adequately cover the evidence for the traditional use of these extracts in the EU for at least 30 years and the non-clinical and clinical safety issues associated with these herbal preparations.

A satisfactory review of the safety data has been provided.

The SmPC, PIL and labelling are satisfactory.

**RISK ASSESSMENT**
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. The risk: benefit balance is acceptable and a Traditional Herbal Registration may be granted.
Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for Sedorma tablets is presented below:
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