Swiss Herbal Remedies Menopause Tincture

THR 35007/0001

UKPAR

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SWISS HERBAL REMEDIES MENOPAUSE TINCTURE

THR 35007/0001

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Swiss Herbal Remedies Ltd a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Swiss Herbal Remedies Menopause Tincture (Traditional Herbal Registration number: THR 35007/0001) on 2 February 2011. This product is available without prescription and can be bought from pharmacies and other outlets.

Swiss Herbal Remedies Menopause Tincture is a traditional herbal medicinal product used for the symptomatic relief of hot flushes associated with the menopause, based on traditional use only. The active ingredient of Swiss Herbal Remedies Menopause Tincture comes from Red peony \( (Paeonia lactiflora \text{ Pallas}) \) root.

This registration is based exclusively upon the longstanding use of Red peony 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 MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Swiss Herbal Remedies Menopause Tincture (THR 35007/0001) to Swiss Herbal Remedies Ltd on 2 February 2011. This product is on the general sales list (GSL).

This application was submitted according to Article 16.c of Directive 2001/83 EC, as amended, as part of the Traditional Herbal Medicines Registration Scheme. The product is used for the symptomatic relief of hot flushes associated with the menopause, based on traditional use only.

The data supplied by the Applicant demonstrate 30 years of traditional use of Red peony, including at least 15 years of use in the European Community. A satisfactory review of the available safety data on Red peony has also been provided, together with an Expert Safety Report supporting the proposed product.
PHARMACEUTICAL ASSESSMENT

HERBAL SUBSTANCE: RED PEONY

Latin name: *Paeonia lactiflora* Pallas
Common name: Chinese peony, Common garden peony, Chi shao yao (Chinese)
Family: Paeoniaceae

The Red peony plants used in this product are sourced from the UK. The roots are collected in spring and autumn, removed from the rhizome and rootlet and dried in the sun (so far as the weather permits) followed by drying in a dedicated dehumidified atmosphere.

Confirmation has been provided that the herbal substance is produced in line with the Guideline on Good Agricultural and Collection Practice (GACP) EMEA/HMPC/246816/2005 and that the herbal substance has organic certification.

Control of Herbal Substance
An appropriate specification based on the BP monograph for White peony root is applied (with reference also made to the Chinese Pharmacopoeia) 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 Directive 2002/72/EC relating to plastic materials and articles intended to come into contact with foodstuffs.

Stability
No stability data have been provided and none are needed due to the short time between harvest and processing. Confirmation has been provided that if this storage period is exceeded the herbal substance will be tested immediately before use for compliance with the herbal substance specification.

HERBAL PREPARATION: RED PEONY ROOT TINCTURE

Parts of the plant used: Root
Ratio of the herbal substance to the herbal preparation (native): 1:3
Extraction solvent: Ethanol 25% v/v

The herbal preparation is an aqueous ethanolic (25% v/v) tincture of the dried herbal substance.

Manufacture
A satisfactory description of the manufacturing process of the herbal preparation and flow diagram 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 this 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 Red peony tincture is acceptable.

**HERBAL PRODUCT: SWISS HERBAL REMEDIES MENOPAUSE TINCTURE**

**Description and Composition of the Herbal Product**
Swiss Herbal Remedies Menopause Tincture is a brown liquid given as oral drops. Each 1 ml of the herbal product contains 1 ml of tincture from dried Red peony root (the herbal preparation). There are no excipients in this product. The ethanol in this product comes from the herbal preparation.

**Manufacture**
A flow diagram outlining the various stages of the manufacturing process and the in-process controls is provided.

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

**Control of Herbal Product**
The finished product specification is satisfactory. 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**
The herbal product is stored in an amber glass bottle fitted with a glass pipette, butyl-rubber bulb and HDPE plastic cap. The plastic cap has a tamper-evident collar that shears on first opening. The bottle size may be 50ml or 100ml.

Suitable specifications have been provided by the packaging suppliers and it has been confirmed that all primary packaging materials comply with Directive 2002/72/EC.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a product shelf-life of 2 years is appropriate when the storage precaution ‘Do not store above 25° C’ is applied.

**Pharmaceutical Expert**
The Quality Overall Summary has been written by a biochemist, with suitable experience.

**Assessor’s comments on the Summary of Product Characteristics, label and Patient Information Leaflet**
All product literature is satisfactory.

A package leaflet has been submitted to the MHRA along with results of consultations 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.

**Assessor’s overall conclusions on quality**
The grant of a Traditional Herbal Registration is acceptable.
NON-CLINICAL ASSESSMENT

NON-CLINICAL ASPECTS
The Expert Safety Report submitted by the applicant lists relevant references to published work studying the toxicology of Red peony root.

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.

Due to a shortage of published data on Red peony root, it is not possible to assess if the safety package for the phytochemical constituents of these active ingredient is acceptable to the standards of today’s GLP and safety testing requirements. However, the information supplied demonstrating traditional use is acceptable and thus the lack of provision of a complete standard safety package is acceptable and in compliance with guideline EMEA/HMPC/32116/05.

Assurance was provided that the results of genotoxicity testing will be provided before renewal of the registration.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
The SPC 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 CPMP/SWP/4447/00.

CONCLUSION
There are no objections to granting of a Traditional Herbal Registration from a non-clinical point of view.
CLINICAL ASSESSMENT

PROPOSED INDICATION
The applicant has submitted the following therapeutic indication:

“A traditional herbal medicinal product used for the symptomatic relief of hot flushes associated with the menopause, based on traditional use only.”

The indication is acceptable.

POSOLOGY AND METHOD OF ADMINISTRATION
The applicant has submitted the following:

“For oral use only

Adult Females
For the symptomatic relief of hot flushes associated with the menopause: Take 20 drops (1 ml) in a small amount of water, three times a day.
There is no relevant use in children and adolescents under 18 years of age.

If symptoms persist, worsen or do not improve during the use of the medicinal product, a doctor or qualified healthcare practitioner should be consulted.”

This is acceptable.

EFFICACY
No clinical efficacy data is required for registration of Traditional Herbal Medicinal Products (THMP).

EVIDENCE OF TRADITIONAL USE
Red peony root is generally accepted to have a tradition of use as an herbal medicine. 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 which shows evidence for the medicinal use of Red peony root for more than 30 years, including at least 15 years within the EU. Therefore, there is sufficient evidence of traditional use of this herbal preparation and a traditional herbal registration can be granted.

SAFETY REVIEW
Article 16 c 1 (d) requires the applicant to provide a bibliography of the safety data together with an expert report.
The safety review has been provided, as well as an expert report written by a professional with relevant expertise. A CV has been included.
The applicant has provided satisfactory information supporting the safety of Red peony root.
ASSESSMENT OF SUITABILITY FOR GSL STATUS
Section 51 of the Medicines Act 1968 states that “GSL may be appropriate for medicines which can, with reasonable safety, be sold or supplied otherwise than by or under the supervision of a pharmacist”. The term “reasonable safety” may usefully be defined as: “Where the hazard to health and the risk of misuse and the need for special precautions in handling are small, and where wider sale would be a convenience to the purchaser”.

1. Hazard to health
There appears to be a minimal risk of hazard to health.

2. Risk of misuse
In essence the risk of misuse of this product is felt to be low.

3. Need to take special precautions in handling

4. Wider sales are convenient to the purchaser
In summary, it is considered that the four above criteria for GSL status have been met and this product should be suitable for GSL status.

PRODUCT LITERATURE
The SPC, PIL and labelling for this product is medically satisfactory.

RECOMMENDATIONS
A Traditional Herbal Registration may be granted.
OVERALL CONCLUSION AND RISK ASSESSMENT

QUALITY
The quality data submitted with this application are satisfactory.

NON-CLINICAL
No new non-clinical data were submitted with this application. However, assurance was provided that the results of genotoxicity testing will be provided before renewal of this registration. This is satisfactory.

EFFICACY AND SAFETY
No clinical efficacy data are required for registration of Traditional Herbal Medicinal Products (THMP).

The Applicant has provided a bibliographic review which shows evidence for the use of Red peony root for a period exceeding 30 years, including at least 15 years within the EU.

A satisfactory review of the safety data has been provided.

The SPC, 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.
## STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the Traditional Herbal Registration application on 15 October 2009
2. Following standard checks and communication with the applicant the MHRA considered the application valid on 29 October 2009
3. Pharmaceutical, preclinical and clinical issues were raised in relation to this application at the Herbal Medicine Advisory Committee meeting on 27 January 2010
4. The applicant addressed the issues raised by the HMAC on 30 July 2010
5. Following assessment of the response the MHRA requested further information relating to the quality and clinical dossiers on 26 August 2010
6. The applicant responded to the MHRA’s requests, providing further information on the dossiers on 7 January 2011
7. A THR was granted on 2 February 2011
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Swiss Herbal Remedies Menopause Tincture

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 1 ml of oral liquid contains 1 ml of tincture from dried Red Peony (Paeonia lactiflora Pallas) root (1:3). Extraction solvent: Ethanol 25% v/v.

Each 1 ml of oral liquid also contains approximately 197 mg Ethanol (alcohol) equivalent to 5 ml of beer or 2 ml of wine.
For a full list of excipients see Section 6.1.

3 PHARMACEUTICAL FORM
Oral drops
A brown liquid

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
A traditional herbal medicinal product used for the symptomatic relief of hot flushes associated with the menopause, based on traditional use only.

4.2 Posology and method of administration
For oral use only

Adult Females
For the symptomatic relief of hot flushes associated with the menopause: Take 20 drops (1 ml) in a small amount of water, three times a day.
There is no relevant use in children and adolescents under 18 years of age.
If symptoms persist, worsen or do not improve during the use of the medicinal product, a doctor or qualified healthcare practitioner should be consulted.

4.3 Contraindications
Patients with known hypersensitivity to Paeonia lactiflora, or any of the excipients.
Pregnancy and lactation (see Section 4.6).

4.4 Special warnings and precautions for use
Do not exceed the stated dose.
Contains alcohol – up to 197 mg ethanol per dose (equivalent to 5 ml of beer or 2 ml of wine).
Harmful for those suffering from alcoholism. To be taken into account in high risk groups such as patients with liver-disease, or epilepsy.
There is no relevant use in children and adolescents under 18 years of age.

If menstrual disorders occur or menstruation re-appears and if symptoms are persistent, of unknown origin, or have recently occurred, a doctor should be consulted.

A study in animals has shown delayed absorption of phenytoin when administered with Peony root. The clinical significance of these findings is unknown. Patients taking phenytoin should consult their doctor before using this product.

### 4.5 Interaction with other medicinal products and other forms of interaction
No studies have been carried out to determine if drug interactions occur with this product.

Contains alcohol, and should therefore be avoided in patients taking other medication known to interact with alcohol (e.g. metronidazole).

### 4.6 Pregnancy and lactation
The safety of this product during pregnancy and lactation has not been established, therefore the use of this product during pregnancy and lactation is not recommended.

### 4.7 Effects on ability to drive and use machines
No studies on the effect of this product on the ability to drive or use machinery have been performed. This product contains alcohol (see Section 2).

### 4.8 Undesirable effects
Stomach upsets.
The frequency is not known.

If other adverse reactions not mentioned above occur, a doctor or qualified healthcare practitioner should be consulted.

### 4.9 Overdose
No case of overdose has been reported.

Overdose of this product may result in alcohol intoxication: the amount in a full bottle: (9.9g in 50ml and 19.8g in 100ml: equivalent to 0.5 and 1.0 large glasses of wine respectively) may result in intoxication and should be treated accordingly.

### 5 PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties
Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

#### 5.2 Pharmacokinetic properties
Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.
5.3 **Preclinical safety data**
Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

6 **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**
Ethanol (from tincture)

6.2 **Incompatibilities**
None known

6.3 **Shelf life**
Two years.

6.4 **Special precautions for storage**
Do not store above 25°C.

6.5 **Nature and contents of container**
Amber glass bottle fitted with glass pipette, butyl-rubber bulb and HDPE plastic cap. Plastic cap includes a tamper-evident collar that shears on first opening: 50ml and 100ml.
Not all pack sizes may be marketed.

6.6 **Special precautions for disposal**
No special requirements.

7 **MARKETING AUTHORISATION HOLDER**
Swiss Herbal Remedies Ltd, St Mary Street, Cardiff, CF10 1AT

8 **MARKETING AUTHORISATION NUMBER(S)**
THR 35007/0001

9 **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
02/02/2011

10 **DATE OF REVISION OF THE TEXT**
02/02/2011
PATIENT INFORMATION LEAFLET

Patient Information Leaflet
Swiss Herbal Remedies Menopause Tincture
Red Peony root tincture

Please read this leaflet carefully before using Swiss Herbal Remedies Menopause Tincture. It contains important information about this product.

Keep this leaflet. You may want to read it again. If you need more information or advice, please ask your doctor, pharmacist or qualified healthcare practitioner.

What is in this leaflet

1. What this product is and what it is used for
2. Before you take this product
3. How to take this product
4. Possible side effects
5. How to store this product
6. Further information

1. What this product is and what it is used for

Swiss Herbal Remedies Menopause Tincture is a traditional herbal medicinal product used for the symptomatic relief of hot flushes associated with the menopause, based on traditional use only.

2. Before you take this product

Do not take this product if you:
- are allergic to any of the ingredients (see Section 6)
- are pregnant or breastfeeding
- are under 18 years of age
- are taking a medicine containing Phenytoin

Tell your doctor if you have an intolerance to any of the ingredients.
No studies on the ability to drive or use machinery whilst taking this product have been performed.

You should also know:
This product contains approximately 197mg of ethanol (alcohol) per dose, equivalent to 5ml beer or 2ml wine. Harmful for people suffering from alcoholism or liver disease.

3. How to take this product

Adult Females:
Take 20 drops (1 ml) in a small amount of water, three times a day.

Do not exceed the stated dose
This product is not recommended for children or those under 18 as there is no relevant indication.

If you take too much of this product (overdose)
If you take more than the recommended dose, speak to a doctor, pharmacist or qualified healthcare practitioner and take this leaflet with you. Overdose of this product may result in alcohol intoxication and should be treated accordingly (see Section 2 - Before you take this product).

If you forget to take this product
Continue to take your usual dose at the usual time. It does not matter if you have missed a dose.

If your symptoms persist, worsen or do not improve during the use of this product, tell your doctor, pharmacist or qualified healthcare practitioner.
If you have any questions, or are unsure about anything, please ask your doctor, pharmacist or qualified healthcare practitioner.

4. Possible side effects

Like all medicines, this product can have side effects, although not everybody gets them.

These include:
- Upset stomach

If this persists or becomes troublesome stop taking the product.
Tell your doctor or pharmacist if you notice any other side effects.

5. How to store this product

Do not use after the expiry date shown on the bottle
Return any out of date medicine to your pharmacist who will dispose of it for you.

Do not store above 25°C. Keep the bottle tightly closed.

Keep all medicines out of the reach and sight of children

6. Further information

Swiss Herbal Remedies Menopause Tincture is a brown liquid.

Ingredients: Each 1 ml of oral liquid contains 1 ml of tincture from dried Red Peony (Paeonia lactiflora Pallas) root (1:3). Extraction solvent: Ethanol 25% v/v. There are no other ingredients in this product.

This product is available in packs of 50ml and 100ml. Not all pack sizes may be marketed.

Traditional Herbal Registration Holder:
Swiss Herbal Remedies, 3 St Mary's Street, Cardiff, CF10 2AT, United Kingdom.

Traditional herbal registration number: THR 35007/0001

Manufacturer:
Rutland Biodynamics Ltd, Town Park Farm, Brooke, RUTLAND, LE15 8DG, United Kingdom.

If you would like further information about this product
Swiss Herbal Remedies has a telephone helpline or an e-mail address if you need further information on this product.

Email - info@swissherbalremedies.com Phone – 02920 417803

Leaflet prepared January 2011

You can help to make medicines safer by reporting any side-effects to the Yellow Card Scheme at www.yellowcard.gov.uk. Alternatively you can get a paper Yellow Card form from your GP’s surgery or pharmacy, or call freephone 0808 100 3352 (available 10am-2pm Monday – Friday).

Certification Mark

MHRA PAR; SWISS HERBAL REMEDIES MENOPAUSE TINCTURE, THR 35007/0001
LABELLING

50 ml bottle:

Label

![Swiss Herbal Remedies Menopause Tincture Label](image)

**Ingredients:**
Each 1 ml of oral liquid contains 1 ml of tincture from dried Red Peony (Paeonia lactiflora Pall.) root (1:3). Extraction solvent Ethanol 35% v/v.

**Do not store above 25°C.**

**Traditional Herbal Registration Holder:**
Swiss Herbal Remedies Ltd,
Cardiff, CF10 1AT

**Traditional Herbal Registration Number:**
THR 35007/0001

**Manufactured by:**
Rutland Biodynamics Ltd, Brooks, Rutland,
LE15 8DG.

**For further information about this product, contact:**
info@swissherbalremedies.com
Tel: 02920 417803

**Directions for use:**
Adult females:
Take 20 drops (1ml) in a small amount of water three times a day.

Do not exceed the stated dose.

Not for use in children or those under 18 or patients taking a medicine containing Phenytoin.

**For oral use only**

Please read the enclosed patient information leaflet before taking this product.

Keep out of the reach and sight of children.

See expiry date on bottle.

**Caution:**
Do not use if you are allergic to any of the ingredients.

This product contains ethanol. Harmful for people suffering from alcoholism. See leaflet for further information.

If symptoms persist or worsen or adverse reactions not mentioned in the leaflet occur, consult a doctor or qualified healthcare practitioner.
100 ml bottle:

Label

Swiss Herbal Remedies

Menopause Tincture

Red Peony root tincture

A traditional herbal medicinal product used for the symptomatic relief of hot flushes associated with the menopause, based on traditional use only.

100 ml

Ingredients:
Each 1 ml of oral liquid contains 1 ml of tincture from dried Red Peony (Paeonia lactiflora Pall) root (1:3). Extraction solvent: Ethanol 25% v/v.

Do not store above 25°C.

Traditional Herbal Registration
Holder: Swiss Herbal Remedies Ltd, Cardiff, CF10 1AT

Traditional Herbal Registration Numbers: THR 35007/0001

Manufactured by: Rutland Biodynamics Ltd, Brockle, Rutland, LE5 6DG.

For further information about this product, contact:
info@swissherbalremedies.com
Tel: 02920 447803

Directions for use:
Adult females: Take 20 drops (1 ml) in a small amount of water, three times a day. Do not exceed the stated dose. Not for use in children or those under 18 or patients taking a medicine containing Phenyle.

For oral use only
Please read the enclosed patient information leaflet before taking this product.
Keep out of the reach and sight of children.
See expiry date on bottle.

Cautions:
Do not use if you are allergic to any of the ingredients.
This product contains alcohol. Harmful for people suffering from alcoholism. See leaflet for further information.
If symptoms persist, or worsen or adverse reactions not mentioned in the leaflet occur, consult a doctor or qualified healthcare practitioner.
Swiss Herbal Remedies

Menopause Tincture
Red Peony Root Tincture

Ingredients: Each 1ml of oral liquid contains 10ml of tincture from dried Red Peony (Paeonia lactiflora Pall) root (1:2). Desiccation solvent: Ethanol 29% v/v.

Directions for use:
Adults: For symptoms of menopausal symptoms. Take 20 drops (1ml) in a small amount of water three times a day.

Caution:
Do not exceed the stated dose. Not for use in children or those under 18 or patients taking a medication containing Phenoxy.

For further information about this product contact:
info@swissherbalremedies.com
Tel: 029 2041 7803