Kalms Sleep

THR 01074/0236

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KALMS SLEEP

THR 01074/0236

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted G.R. Lane Health Products Limited a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Kalm s Sleep (Traditional Herbal Registration number: THR 01074/0236) on 05 March 2013. Kalms Sleep is available without prescription and can be bought from pharmacies and other outlets.

Kalms Sleep is a traditional herbal medicinal product used for the temporary relief of sleep disturbances, based on traditional use only.

This registration is based exclusively upon evidence of the use of Verbena Herb, Hop strobiles and dry extract of Passion Flower herb, Wild Lettuce 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 the 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.
KALMS SLEEP

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Kalms Sleep (Traditional Herbal Registration number: THR 01074/0236) on 05 March 2013. This product is on the general sales list (GSL).

A product licence (PL 01074/0026) was originally granted to G.R. Lane Health Products Limited on 17 June 2005. G.R. Lane Health Products Limited has committed to cancel PL 01074/0026 following the grant of the Traditional Herbal Registration Certificate.

This THR application was made under Article 16.c of Directive 2001/83 EC in accordance with arrangements to transfer certain herbal products with a Marketing Authorisation to a THR (according to MHRA Guidance dated January 2009). The application falls within the simplified THR application Category A, as no significant changes have been made to the formulation of the product. No new data were submitted, nor was it necessary for this application, as the data are essentially identical to those of the existing product.
PHARMACEUTICAL ASSESSMENT

HERBAL SUBSTANCE: VERBENA HERB

Scientific name of the plant: *Verbena officinalis* (L.)
Plant family: Verbenaceae

The herbal substance is acceptable.

HERBAL PREPARATION: VERBENA HERB

The herbal substance is processed into powdered form and immediately transferred for use in the manufacture of the tablets, therefore control, packaging and storage of the herbal preparation is not considered relevant in this application. This is consistent with the already licensed product and is therefore acceptable.

HERBAL SUBSTANCE: VALERIAN ROOT

Scientific name of the plant: *Valeriana officinalis* (L.)
Plant family: Valerianaceae

The herbal substance is acceptable.

HERBAL PREPARATION: VALERIAN ROOT

Extraction solvent: Ethanol 60% V/V

The herbal preparation specification is in line with that applied to the herbal preparation used in the already licensed product. It is, therefore, acceptable.

HERBAL SUBSTANCE: HOP STROBILES

Scientific name of the plant: *Humulus lupulus* (L.)
Plant family: Cannabidaceae

The herbal substance is acceptable.

HERBAL PREPARATION: HOP STROBILES

The herbal substance is processed into powdered form and immediately transferred for use in the manufacture of the tablets, therefore control, packaging and storage of the herbal preparation is not considered relevant in this application. This is consistent with the already licensed product and is therefore acceptable.

HERBAL SUBSTANCE: WILD LETTUCE LEAF

Scientific name of the plant: *Lactuca virosa* (L)
Plant family: Asteraceae
Synonyms: Bitter lettuce
The herbal substance is acceptable.

**HERBAL PREPARATION:** WILD LETTUCE LEAF

- **Drug extract ratio (DER):** 4:1
- **Extraction solvent:** Methanol 50% V/V

The herbal preparation specification is in line with that applied to the herbal preparation used in the already licensed product. It is, therefore, acceptable.

**HERBAL SUBSTANCE:** PASSION FLOWER HERB

- **Scientific name of the plant:** Passiflora incarnata (L.)
- **Plant family:** Passifloraceae

The herbal substance is acceptable.

**HERBAL PREPARATION:** PASSION FLOWER HERB

- **Drug extract ratio (DER):** 5.35:1
- **Extraction solvent:** Ethanol 60% V/V

The herbal preparation specification is in line with that applied to the herbal preparation used in the already licensed product. It is, therefore, acceptable.

**HERBAL PRODUCT:** KALMS SLEEP

**Description and Composition of the Herbal Product**

Kalms Sleep tablets are dark grey, round, biconvex sugar-coated tablets. Each sugar-coated tablet contains:

- 60 mg of Verbena Herb,
- 34.65 mg of dry extract from Valerian root,
- 30 mg Hop strobiles,
- 22.5 mg of dry extract from Wild Lettuce leaf and
- 16.82 mg of dry extract from Passion Flower herb

and the pharmaceutical excipients maltodextrin, colloidal anhydrous silica, cellulose, gum arabic, acacia, spray-dried, calcium hydrogen phosphate, croscarmellose sodium, icing sugar, magnesium stearate, stearic acid, calcium carbonate (Light), Mastercote Grey SP0933, Opaglos 6000, talc, shellac varnish, sucrose and titanium dioxide. The formulation is in line with that of the already licensed product. It is, therefore, acceptable.

**Manufacture**

The manufacturing process is in line with that of the already licensed product and is satisfactory.

**Finished Product Specification**

The finished product specification is in line with that of the already licensed product and is satisfactory.

**Container Closure System**

Kalms Sleep is stored in:

- Amber glass jars with foil tamper-evident seals and a white polypropylene screw-cap.
• Amber glass bottles (USP Type III glass) fitted with a white high-density polyethylene (HDPE) tamper evident cap.

Pack sizes of 50 and 84 tablets have been authorised for both product presentation types, although not all pack sizes may be marketed. Both types of packaging have been used to store the already licensed product and are satisfactory.

**Stability**
The product has a shelf-life of 3 years when the storage precautions ‘Do not store above 25°C’ and ‘Store in the original package’ are applied (for both product presentation types). This is in line with the already licensed product and is appropriate.

**Summary of Product Characteristics, product labels and Patient Information Leaflet**
All product literature is in line with that of the already licensed product, with some details amended in line with other products registered under the THR scheme.

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 CONCLUSION**
It is recommended that a Traditional Herbal Registration can be granted.
PRECLINICAL ASSESSMENT

INTRODUCTION
No new preclinical data have been supplied with this application and none are required for an application of this type.

Assurance has been given that the results of genotoxicity testing will be provided by the renewal date of the Traditional Herbal Registration.

PRODUCT LITERATURE
All product literature is satisfactory from a preclinical point of view.

ASSESSOR’S OVERALL CONCLUSION
It is recommended that a Traditional Herbal Registration can be granted.
CLINICAL ASSESSMENT

INTRODUCTION
The clinical particulars for Kalms Sleep are identical to those for the already licensed product. This is satisfactory.

PRODUCT LITERATURE
All product literature is medically satisfactory.

ASSESSOR’S OVERALL CONCLUSION
It is recommended that a Traditional Herbal Registration can be granted.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
Kalms Sleep is identical to an already licensed product. It is, therefore, pharmacetically satisfactory.

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type. The results of genotoxicity testing will be provided before the THR is renewed.

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

SAFETY
No new or unexpected safety concerns arose from this application.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The benefit: risk balance is acceptable and a THR should be granted.
KALMS SLEEP

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**STEPS TAKEN FOR ASSESSMENT**

1. The MHRA received the Traditional Herbal Registration application on 25 January 2013.
2. Following standard checks and communication with the applicant the MHRA considered the application valid on 30 January 2013.
3. Following assessment of the application the MHRA requested further information relating to the dossier on 12 February 2013.
4. The applicant responded to the MHRA’s requests, providing further information on the dossier on 04 March 2013.
5. A THR was granted on 05 March 2013.
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Kalms Sleep

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each coated tablet contains:
60 mg Verbena Herb (*Verbena officinalis* L.)

34.65 mg of extract (as dry extract from Valerian root (*Valeriana officinalis* L.) (equivalent to 139 to 173mg of Valerian root)
Extraction solvent: Ethanol 60% v/v

30 mg Hop strobiles (*Humulus lupulus* L.)

22.5 mg of extract (as dry extract from Wild Lettuce leaf (*Lactuca virosa* L.) (equivalent to 90 mg of Wild Lettuce leaf).
Extraction solvent: Methanol 50% v/v

16.82 mg of extract (as dry extract from Passion Flower herb (*Passiflora incarnata* L.) (equivalent to 90 mg of Passion Flower herb).
Extraction solvent: Ethanol 60% v/v

Each coated tablet contains 168 mg sucrose.
(see section 4.4 ‘Special warnings and precautions for use.’)

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Coated tablet.
Dark grey, round biconvex sugar coated tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
A traditional herbal medicinal product used for the temporary relief of sleep disturbances, based on traditional use only.

4.2 Posology and method of administration
For oral short term use only.
Adults and the elderly: Take 3 or 4 tablets one hour before bedtime.

Not recommended for use in children or adolescents under 18 years old (see Section 4.4 Special warnings and precautions for use’).

As treatment effects may not be apparent immediately, Kalms Sleep should be taken for 2-4 weeks continuously.
Duration of use:
If symptoms worsen or do not improve after 4 weeks, a doctor or a qualified healthcare practitioner should be consulted.

4.3 Contraindications
Hypersensitivity to the active substances or to any of the excipients.

4.4 Special warnings and precautions for use
Do not exceed the stated dose.

Contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

The use of this product in children or adolescents under 18 years of age is not recommended because data are not sufficient and medical advice should be sought.

If symptoms worsen or do not improve after 4 weeks, a doctor or a qualified healthcare practitioner should be consulted.

4.5 Interaction with other medicinal products and other forms of interaction
Only limited data on pharmacological interactions with other medicinal products are available. Clinically relevant interactions with drugs metabolised by the CYP 2D6, CYP 3A4/5, CYP 1A2 or CYP 2E1 pathway have not been observed.

Additive effects with hypnotics and other sedative cannot be excluded and therefore co-medication is not recommended as a general precaution.

The effect of Kalms Sleep may be potentiated by alcohol. Excessive concomitant consumption of alcohol should therefore be avoided.

4.6 Fertility, pregnancy and lactation
Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Studies on the effects on fertility have not been performed.

4.7 Effects on ability to drive and use machines
May impair the ability to drive and use machines. If affected, do not drive or operate any tools or machines.

4.8 Undesirable effects
Gastrointestinal symptoms, such as nausea, abdominal cramps, may occur after ingestion of Valerian root preparations. The frequency is not known.

One case of hypersensitivity (vasculitis) and one case of tachycardia have been reported with Passion Flower. 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
Valerian root at a dose of approximately 20 g (equivalent to 111 tablets) caused benign symptoms (fatigue, abdominal cramp, chest tightness, lightheadedness, hand tremor and mydriasis), 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 30g of the drug) withdrawal symptoms (delirium) have been reported.

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
- Extract
- Maltodextrin
- Colloidal anhydrous silica
- Cellulose
- Gum Arabic

Core:
- Acacia, Spray-dried
- Calcium Hydrogen Phosphate
- Croscarmellose Sodium
- Icing Sugar
- Magnesium Stearate
- Stearic Acid

Coating:
- Acacia, Spray-dried
- Calcium Carbonate (Light)
- Mastercote Grey SP0933
- Opaglos 6000
- Talc
- Shellac Varnish
- Sucrose
Titanium Dioxide

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
Do not store above 25ºC.
Store in the original package

6.5 Nature and contents of container
50 or 84 tablets in amber glass jars with foil tamper-evident seals and white polypropylene screw-caps.
50 or 84 tablets in amber glass bottles (USP type III glass) with white HDPE tamper evident caps.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements

7 MARKETING AUTHORISATION HOLDER
G. R. Lane Health Products Limited
Sisson Road
Gloucester
GL2 0GR
United Kingdom
Tel: +44 (0)1452 524012
Fax: +44 (0)1452 507930
Email: info@laneshealth.com

8 MARKETING AUTHORISATION NUMBER(S)
THR 01074/0236

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATION
05/03/2013

10 DATE OF REVISION OF THE TEXT
05/03/2013
PATIENT INFORMATION LEAFLET

PACKAGE LEAFLET

Kalms Sleep tablets
Read all of this leaflet carefully because it contains important information for you. This medicine is available without prescription. However you still need to take Kalms Sleep tablets carefully to get the best results from them.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve after 4 weeks.
- If any of the side effects become serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Kalms Sleep tablets are and what they are used for
2. Before you take Kalms Sleep tablets
3. How to take Kalms Sleep tablets
4. Possible side effects
5. How to store Kalms Sleep tablets
6. Further information

1. What Kalms Sleep is and what it is used for
Kalms Sleep contains a combination of herbs. It is a traditional herbal medicinal product used for the temporary relief of sleep disturbances, based on traditional use only...

2. Before you take Kalms Sleep tablets
Do not take Kalms Sleep if you:
- are allergic to any of the ingredients (see Section 6 for a complete list of ingredients).
- are pregnant or breast feeding
- are under 18
- are already taking a medicine for sleep and anxiety

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including:
- medicines obtained without a prescription.

Important information about some of the ingredients:
This medicine contains sucrose. If you have been told by your doctor that you have an intolerance to some sugars, consult your doctor before taking this product.

Driving and using machines: If you feel sleepy, do not drive or operate machines.

Additional information: The effects of this medicine may be increased by alcohol. Therefore alcohol should be avoided whilst taking this medicine.
3. How to take Kalms Sleep tablets

For the temporary relief of sleep disturbances

**Adults and the elderly** : Take 3 to 4 tablets 60 minutes before bedtime.

The tablets should be swallowed whole with some water or other liquid.

The use in children and adolescents under 18 years of age is not recommended.

As the effects of this product may not occur immediately, the tablets should be taken continuously for 2-4 weeks.

If symptoms worsen or do not improve after 4 weeks, a doctor or a qualified healthcare practitioner should be consulted.

**If you take more Kalms Sleep tablets than you should**
If you take too many tablets, consult your doctor or qualified healthcare practitioner as soon as possible. Take this leaflet to show them.

**If you forget to take Kalms Sleep tablets**
Do not take a double dose to make up for a missed dose.
If you are unsure about anything, consult your doctor or qualified healthcare practitioner for advice.

4. Possible side effects
Like all medicines, Kalms Sleep tablets can cause side effects, although not everybody gets them.

Gastrointestinal effects such as nausea, stomach cramps have been reported with Valerian root preparations. The frequency is not known.

One case of hypersensitivity (vasculitis) and one case of increased heart beat (tachycardia) have been reported in patients using Passion flower herb. The frequency is not known.

If any of the side effects become serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

You can help make medicines safer by reporting any side effects to the Yellow Card Scheme at www.mhra.gov.uk/yellowcard. Alternatively you can get a paper Yellow Card form from your GP's surgery or pharmacy or call freephone 0808 100 3352

5. How to store Kalms Sleep tablets
Keep out of the reach and sight of children.
Do not take these tablets after the expiry date which is stated on the outer carton and container.
Do not store above 25°C.
Store in the original package.

6. Further Information

What Kalms Sleep tablets contains

The active substance per tablet is:

Verbena Herb (*Verbena officinalis* L.) .......................................................... 60mg

Hop strobiles (*Humulus lupulus* L.) .............................................................. 30mg

Dry extract from Passion Flower herb (*Passiflora incarnata* L.)
(equivalent to 90 mg of Passion Flower herb)
Extraction solvent: Ethanol 60% v/v............................................................... 16.82mg

Dry extract from Wild Lettuce (*Lactuca virina* L.)
(equivalent to 29 mg of Wild Lettuce leaf)
Extraction solvent: Water .................................................................................. 22.5mg

Dry extract from Valerian root (*Valeriana officinalis* L.)
(equivalent to 139 to 173 mg of Valerian root)
Extraction solvent: Ethanol 60% v/v............................................................... 34.65mg

The other ingredients are:

Extract: Maltodextrin, Colloidal anhydrous silica, Cellulose, Gum Arabic.
Core: Acacia, Calcium Hydrogen Phosphate, Croscarmellose Sodium, Icing Sugar,
Magnesium Stearate, Stearic Acid
Coating: Acacia, Calcium Carbonate (Light), Mastercote Grey SP0933, Opaglos 6000
Talc, Shellac Varnish, Sucrose, Titanium Dioxide

What Kalms Sleep tablets looks like and contents of the pack

Kalms Sleep tablets are dark grey round sugar coated tablets. They are available in amber glass bottles containing 50 or 84 tablets.
Traditional Herbal Registration Holder and Manufacturer
G. R. Lane Health Products Limited
Sisson Road
Gloucester
GL2 0GR
United Kingdom
Tel: +44 (0)1452 524012
Email: info@laneshealth.com
This leaflet was last revised 03/2013

For a large print, Braille or audio versions of this leaflet please telephone: 01452 524012.
LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT
   Kalms Sleep

2. STATEMENT OF ACTIVE SUBSTANCE(S)
   Each coated tablet contains:
   60 mg Verbena Herb (Verbena officinalis L.)
   34.65 mg of extract (as dry extract from Valerian root (Valeriana officinalis L.)
   (equivalent to 139 to 173mg of Valerian root)
   Extraction solvent: Ethanol 60% v/v
   30 mg Hop strobiles (Humulus lupulus L.)
   22.5 mg of extract (as dry extract from Wild Lettuce leaf (Lactuca virosa L.)
   (equivalent to 90 mg of Wild Lettuce leaf).
   Extraction solvent: Methanol 50% v/v
   16.82 mg of extract (as dry extract from Passion Flower herb (Passiflora incarnata
   L.) (equivalent to 90 mg of Passion Flower herb).
   Extraction solvent: Ethanol 60% v/v

3. LIST OF EXCIPIENTS
   Also contains sucrose (see leaflet for further information)

4. PHARMACEUTICAL FORM AND CONTENTS
   50 or 84 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION
   For temporary relief of sleep disturbances;
   Adults and the elderly: Take 3 or 4 tablets one hour before bedtime.
   Not recommended for use in children or adolescents under 18 years old.

6. SPECIAL WARNING THAT THE MEDICAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN
Keep out of the reach and sight of children.
Do not exceed the stated dose.

7. OTHER SPECIAL WARNING(S), IF NECESSARY
Do not take:
• if you are allergic to any of the ingredients
• if you are pregnant or breast feeding
• if you are under 18
• if you are already taking a medicine for sleep and anxiety

If you feel sleepy, do not drive or operate machines.

Alcohol may increase the sedative effects, therefore excessive alcohol consumption should be avoided.

If symptoms worsen or do not improve after 4 weeks consult your doctor.
Read enclosed leaflet before use

8. EXPIRY DATE
EXP: mm/yyyy
Do not use after the expiry date shown on the carton and container/blister strip

9. SPECIAL STORAGE CONDITIONS
Do not store above 25°C.
Store in the original package.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE
Not applicable

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER
G. R. Lane Health Products Limited
Sisson Road
Gloucester
GL2 0GR
United Kingdom

12. MARKETING AUTHORISATION NUMBER
THR 01074/0236
13. **MANUFACTURER'S BATCH NUMBER**

BN: xxxxx

14. **GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product not subject to medical prescription

15. **INSTRUCTIONS ON USE**

A traditional herbal medicinal product used for the temporary relief of sleep disturbances, based on traditional use only

Adults and the elderly: Take 3 or 4 tablets one hour before bedtime.

Not recommended for use in children or adolescents under 18 years old.