# Valerina Day-Time film-coated tablets

**THR 15525/0007**

**UKPAR**

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The Medicines and Healthcare products Regulatory Agency (MHRA) granted Pharbio Medical International AB a Traditional Herbal Registration certificate for the traditional herbal medicinal product Valerina Day-Time film-coated tablets (Traditional Herbal Registration number: THR 15525/0007). This product is available without prescription and can be bought from pharmacies and other outlets.

Valerina Day-Time film-coated tablets is a traditional herbal medicinal product used for the temporary relief of symptoms of mild anxiety. The active ingredients in Valerina Day-Time film-coated tablets come from the roots of the Valerian plant (*Valeriana officinalis* L.) and the leaves of the Lemon Balm plant (*Melissa officinalis* L.)

This registration is based exclusively upon evidence of the use of Valerian root and Lemon Balm leaf as traditional herbal medicines 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.
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INTRODUCTION

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Valerina Day-Time film-coated tablets (THR 15525/0007) to Pharbio Medical International AB on 19 November 2010. This product is on the general sales list (GSL).

A product licence (PL 11357/0001) was granted to Medic Herb UK Ltd for this product on 25 March 1993. Following a change of ownership on 18 April 2007 the product licence was transferred to Pharbio Medical International AB under product licence number PL 15525/0001. Confirmation is given that PL 15525/0001 will be cancelled after the THR is granted.

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 (product licence) to a THR (according to MHRA Guidance dated January 2009). The application falls within the simplified THR application Category A as no 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: VALERIAN ROOT

Scientific name of the plant: Valeriana officinalis L.
Family: Valerianaceae
Synonyms of the herbal substance: Valerian
Parts of the plant used: root

The herbal substance complies with the Ph. Eur. monograph, it is, therefore, acceptable.

HERBAL PREPARATION: VALERIAN ROOT DRY EXTRACT

Herbal preparation: Valerian root dry extract
Parts of the plant used: 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: LEMON BALM LEAF

Scientific name of the plant: Melissa officinalis L.
Family: Lamiaceae
Synonyms of the herbal substance: Lemon Balm
Parts of the plant used: leaf

The herbal substance complies with the Ph. Eur. monograph, it is, therefore, acceptable.

HERBAL PREPARATION: LEMON BALM LEAF DRY EXTRACT

Herbal preparation: Lemon balm leaf dry extract
Parts of the plant used: leaf
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: VALERINA DAY-TIME FILM-COATED TABLETS

Description and Composition of the Herbal Product
Valerina Day-Time film-coated tablets are round, biconvex, pale yellow, film-coated tablets. The tablets contain the excipients cellulose, colloidal anhydrous silica dioxide,
lactose monohydrate, potato starch, calcium hydrogen phosphate, magnesium stearate, hypromellose, titanium dioxide, macrogol 6000 and betacarotene. The formulation is identical to 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**
The tablets are stored in foil strip blister packs packed in a cardboard carton. Each cardboard carton of 40, 60 or 80 tablets consists of 2x20, 3x20 or 4x20 foil strip blister packs, respectively. This type of packaging has been used to store the already licensed product and is satisfactory.

**Stability**
The product shelf-life of 2 years was applied to the already licensed product and is appropriate when the storage precautions ‘do not store above 25°C’ and ‘keep in original package’ are applied.

**Summary of Product Characteristics, label 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 valerian-containing 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 Conclusions on Quality**
The grant of a Traditional Herbal Registration is acceptable.
PRECLINICAL ASSESSMENT

INTRODUCTION
No new preclinical data have been supplied with this application and none is 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 THR.

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

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

INTRODUCTION
The clinical particulars for Valerina Day-Time film-coated tablets are identical to those for the already licensed product. This is satisfactory.

PRODUCT LITERATURE
All product literature is medically satisfactory.

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

QUALITY
Valerina Day-Time film-coated tablets is identical to an already licensed product. It is, therefore, pharmaceutically 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 (THMP).

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

RISK ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified.
VALERINA DAY-TIME FILM-COATED TABLETS

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STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the Traditional Herbal Registration application on 26 April 2010
2. Following standard checks and communication with the applicant the MHRA considered the application valid on 27 May 2010
3. Following assessment of the application the MHRA requested further information relating to the dossier on 22 July 2010
4. The applicant responded to the MHRA’s requests, providing further information on the dossier on 16 November 2010
5. A THR was granted on 19 November 2010
1 NAME OF THE MEDICINAL PRODUCT
Valerina Day-Time film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
1 film-coated tablet contains:
100 mg of extract (as dry extract) (4:1) equivalent to 400 mg of Valerian root
(Valeriana officinalis L.).
Extraction solvent: Ethanol 60% V/V.

50 mg of extract (as dry extract) (6.5:1) equivalent to 325 mg of Lemon Balm leaf (Melissa officinalis L.).
Extraction solvent: Ethanol 60% V/V.

Excipient(s): One tablet contains 319 mg of Lactose monohydrate.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film-coated tablet

Round, biconvex, pale yellow tablets.

4 CLINICAL PARTICULARS

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

4.2 Posology and method of administration
For oral short term use only.

Adults and the elderly
2 tablets up to 3 times daily.

The tablets should be swallowed whole with liquid.

As treatment effects may not be apparent immediately, Valerina Day-Time should be taken for at least 2 - 4 weeks continuously.

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

Not recommended for children or adolescents under 18 years of age (see Section 4.4. Special warnings and precautions for use).
4.3 Contraindications
Hypersensitivity to Valerian, Lemon Balm or to any of the excipients.

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

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

One tablet contains 319 mg of Lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction
Valerian extract: Only limited data on pharmacological interactions with other medicinal products are available. Clinically relevant interaction with drugs metabolised by the CYP 2D6, CYP 3A4/5, CYP1A2 or CYP 2E1 pathway has not been observed.

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

Lemon Balm extract: No data on interactions are presently known.

The effect of the product may be potentiated by alcohol. Excessive consumption of alcohol should therefore be avoided.

4.6 Pregnancy and lactation
Safety during pregnancy and lactation has not been established. Due to the lack of data, use during pregnancy and lactation is not recommended.

4.7 Effects on ability to drive and use machines
May impair the ability to drive and use machines. If affected, patients should not drive or operate machinery.

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

There are no known adverse reactions with Lemon Balm.

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

4.9 Overdose
Valerina Day-Time: No cases of overdoses have been reported.
Valerian root at a dose of approximately 20 g (equivalent to 50 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 30 g of the drug) withdrawal symptoms (delirium) have been reported.

Lemon Balm extract: No cases of overdose have been reported. Symptomatic and supportive measures should be taken as appropriate.

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
Melissa extract: Data from in vitro and animal studies indicate that a water extract of Melissa officinalis may inhibit the activity of thyroid stimulating hormone (TSH). The clinical relevance of these findings is not known.

Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed with the Valerian and Melissa extracts.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Extract excipients
Cellulose
Colloidal anhydrous silica dioxide
Lactose monohydrate

Tablet core
Lactose monohydrate
Potato Starch
Calcium Hydrogen Phosphate
Magnesium Stearate

Tablet coating
Hypromellose
Titanium Dioxide
Macrogol 6000
Betacarotene
6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years

6.4 Special precautions for storage
Do not store above 25°C. Keep in original package.

6.5 Nature and contents of container
Each cardboard carton of 40 tablets consists of 2x20 foil strip blister packs
Each cardboard carton of 60 tablets consists of 3x20 foil strip blister packs
Each cardboard carton of 80 tablets consists of 4x20 foil strip blister packs
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER
Pharbio Medical International AB
Box 715
SE-194 27
Upplands Väsby
Sweden

8 MARKETING AUTHORISATION NUMBER(S)
THR 15525/0007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
19/11/2010

10 DATE OF REVISION OF THE TEXT
19/11/2010
Package leaflet: Information for the user

Valerina Day-Time film-coated tablets

Extracts of valerian root and lemon balm leaf

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 Valerina Day-Time carefully to get the best results from it.

- 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 or qualified healthcare practitioner if your symptoms worsen or do not improve after 4 weeks.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or qualified healthcare practitioner.

In this leaflet:
1. What Valerina Day-Time is and what it is used for
2. Before you take Valerina Day-Time
3. How to take Valerina Day-Time
4. Possible side effects
5. How to store Valerina Day-Time
6. Further information

1. What Valerina Day-Time is and what it is used for

Valerina Day-Time is a traditional herbal medicinal product used for the temporary relief of symptoms of mild anxiety based on traditional use only. The tablets contain extracts of valerian root and lemon balm leaf. For full details see section 6.

2. Before you take Valerina Day-Time

Do not take Valerina Day-Time if you are:
- allergic (hypersensitive) to valerian, lemon balm or any of the other ingredients of Valerina Day-Time.
- already taking other medicines for anxiety or sleep.
- under 18 years of age.
- pregnant or breast feeding.

This product contains lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars do not take Valerina Day-Time.

Taking other medicines

Please tell your doctor or qualified healthcare practitioner if you are taking any other medicines.

Alcohol

The effects of Valerina Day-Time may be increased by alcohol. Therefore, you should not drink excessive amounts of alcohol.

3. How to take Valerina Day-Time

For oral short term use only.

Take Valerina Day-Time as advised in this leaflet. You should check with your doctor or qualified healthcare practitioner if you are not sure.

Do not exceed the stated dose.

Adults and the elderly

Take 2 tablets 3 times a day. Swallow the tablets whole with water.

You may need to take the tablets for 2 to 4 weeks continuously to get the effect from the treatment.

Stop taking Valerina Day-Time and contact your doctor or qualified healthcare practitioner if your symptoms worsen or do not improve after 4 weeks.

Children and adolescents

Do not use in children and adolescents under 18 years of age.

If you take more Valerina Day-Time than you should

If you take more than the recommended dose, speak to a doctor, pharmacist or qualified healthcare practitioner and take this leaflet with you.

4. Possible side effects

Like all medicines, Valerina Day-Time can cause side effects, although not everybody gets them.

Stop taking Valerina Day-Time and contact your doctor if you experience any of the following:
- Rash, swallowing or breathing problems, swelling of your lips, face, throat and tongue, feeling faint. These could be signs of an allergic reaction.
- Other side effects include feeling sick and stomach cramps.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or qualified healthcare practitioner.

Driving and using machines

Valerina Day-Time may cause drowsiness. If after taking Valerina Day-Time you feel drowsy, do not drive, use tools or operate machinery.

If you forget to take Valerina Day-Time

Continue to take your usual dose at the usual time. It does not matter if you have missed a dose. Do not take a double dose to make up for forgotten tablets.

If you have any further questions on the use of this product, ask your doctor or qualified healthcare practitioner.
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 0800 100 3352 (available 10 am–2 pm Monday–Friday).

5. How to store Valerina Day-Time
Do not store above 25°C. Keep in the original package to protect the tablets from light and moisture. Keep out of the reach and sight of children.
Do not use Valerina Day-Time after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
Medicines should not be disposed of via wastewater or household waste. Take the medicines no longer required to your pharmacist who will dispose of them. These measures will help to protect the environment.

6. Further information
What Valerina Day-Time contains
- Each film-coated tablet contains:
  100 mg of extract (as dry extract) (4:1) equivalent to 400 mg of Valerian root (Valeriana officinalis L.).
  Extraction solvent: Ethanol 60% V/V.
  50 mg of extract (as dry extract) (6:5:1) equivalent to 325 mg of Lemon Balm leaf (Melissa officinalis L.).
  Extraction solvent: Ethanol 60% V/V.
- The other ingredients are 319 mg of lactose monohydrate, cellulose, colloidal anhydrous silica, potato starch, calcium hydrogen phosphate, magnesium stearate, hypromellose, macrogol 6000, titanium dioxide (E171) and B-carotene (E160a).

What Valerina Day-Time looks like and contents of the pack
The film-coated tablets are pale yellow and round.
Pack sizes: 40, 60, 80 tablets in blisters. Not all pack sizes may be marketed.

Traditional Herbal Registration Holder
Pharbio Medical International AB,
Box 715, SE-194 27 Upplands Väsby, Sweden.
Telephone: +46 8 590 963 00
Email: regulatory@cederroth.com

Manufacturer
Cederroth International Production
Paramedical A/S, Yassingerødevej 3-7,
DK-3540 Lyngby, Denmark.

This leaflet was last approved in November 2010

Self-Help Health education to Relieve Stresses and Strains
- Exercise: gentle exercise can help the body burn up excess energy caused by the adrenaline released at times of stress.
- Self massage: rubbing a tense forehead or neck is a common relaxation method.
- Healthy eating: a varied well balanced diet will help ensure the body receives the essential vitamins and minerals it needs to function at its best. Try to avoid excess intake of coffee, tea or alcohol.
- Heat: some people find saunas or Turkish baths relaxing but simply allowing time for a long hot bath can be an ideal way to relax.
**LABELLING**

**Blister:**

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