LOWATER

THR 00904/0002

UKPAR

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LOWATER

THR 00904/0002

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Kerbina Limited (trading as Bio-Health Limited) a Traditional Herbal Registration Certificate for the traditional herbal medicinal product LOWATER (Traditional Herbal Registration number: THR 00904/0002) on 27 March 2013. LOWATER is available without prescription and can be bought from pharmacies and other outlets.

LOWATER is a traditional herbal medicinal product used to relieve bloating associated with premenstrual water retention, based on traditional use only. The active ingredients in LOWATER come from the leaf of the Buchu plant (Agathosma betulina (Berg) Pillans), the leaf of the Uva Ursi plant (Arctostaphylos uva-ursi (L.) Spreng.) and the root of the Dandelion plant (Taraxacum officinale Weber ex Wigg.)

This registration is based exclusively upon evidence of the use of Buchu leaf, Uva Ursi leaf and Dandelion root 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 LOWATER (THR 00904/0002) to Kerbina Limited (trading as Bio-Health Limited) on 27 March 2013. This product is on the general sales list (GSL).

A product licence of right (PLR) was originally granted to Kerbina Limited for this product. The PLR was reviewed and a product licence (PL 00904/5069R) was granted to Kerbina Limited on 28 April 1988. Kerbina Limited cancelled PL 00904/5069R 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: BUCHU LEAF

Scientific name of the plant: *Agathosma betulina* (Berg) Pillans
Plant family: Rutaceae

The herbal substance is controlled by a suitable specification.

HERBAL PREPARATION: BUCHU LEAF DRY EXTRACT

Drug extract ratio (DER): 4:1
Extraction solvent: Ethanol 70% 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: UVA URSI LEAF

Scientific name of the plant: *Arctostaphylos uva-ursi* (L.) Spreng.
Plant family: Ericaceae

The herbal substance is controlled by a suitable specification.

HERBAL PREPARATION: BUCHU LEAF DRY EXTRACT

Drug extract ratio (DER): 2·5-4·5:1
Extraction solvent: Water

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: DANDELION ROOT

Scientific name of the plant: *Taraxacum officinale* Weber ex Wigg.
Plant family: Asteraceae

The herbal substance is controlled by a suitable specification.

HERBAL PREPARATION: DANDELION ROOT DRY EXTRACT

Drug extract ratio (DER): 2·5-4·5:1
Extraction solvent: Ethanol 70% 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: LOWATER

Description and Composition of the Herbal Product
The herbal product is a grey, bi-convex, coated tablet. Each tablet contains 30 mg of dry extract from Buchu leaf, 30 mg of dry extract from Uva Ursi leaf and 50 mg of dry extract) from Dandelion root. The tablets also contain the pharmaceutical excipients maltodextrin, colloidal anhydrous silica, sucrose, lactose monohydrate, talc, magnesium stearate, sodium starch glycolate, cayenne, titanium dioxide (E171), iron oxide black (E172) and syrup.

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
The tablets are stored in 100ml HDPE polythene containers with a tamper evident cap closure. Pack sizes of 30 or 60 tablets have been authorised. This type of packaging has been used to store the already licensed product and is satisfactory.

Stability
The product has a shelf-life of 3 years when the storage precautions ‘Store below 25ºC’ and ‘Store in the original package’ are applied. 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.

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 LOWATER 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
LOWATER 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.

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.
### STEPS TAKEN FOR ASSESSMENT

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the Traditional Herbal Registration application on 18 March 2013</td>
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<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 26 March 2013</td>
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<td>3</td>
<td>Following assessment of the application the MHRA requested further information relating to the dossier on 1 March 2013</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s request, providing further information on the dossier on 19 March 2013</td>
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<td>5</td>
<td>A THR was granted on 27 March 2013</td>
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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
LOWATER

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each coated tablet contains:
30 mg of extract (as dry extract) from Buchu leaf (*Agathosma betulina* (Berg) Pillans (4:1)
Extraction solvent: Ethanol 70% v/v
30 mg of extract (as dry extract) from Uva Ursi leaf (*Arctostaphylos uva-ursi* (L.) Spreng. (2:5 - 4:5:1)
Extraction solvent: Water
50 mg of extract (as dry extract) from Dandelion root (3:5:1) (*Taraxacum officinale* Weber ex Wigg.)
Extraction solvent: Ethanol 60% v/v
Each tablet contains 228 mg of sucrose and 68 mg lactose
(See section 4.4 special warnings and precautions for use).
For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Coated tablet. Grey bi-convex tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
A traditional herbal medicinal product used to relieve bloating associated with premenstrual water retention, based on traditional use only.

4.2 Posology and method of administration
For oral short term use only
Adults: Two tablets to be taken in the morning and two tablets in the evening. The tablets should be taken before the period is expected to start.
The use in children and adolescents under 18 years of age and the elderly is not recommended (see section 4.4 Special warnings and precautions for use.)
Duration of Use:-
If symptoms worsen or persist after using the product for one week, a doctor or qualified healthcare practitioner should be consulted.

4.3 Contraindications
Hypersensitivity to the active substances or plants of the Asteraceae (Compositae) or to any of the excipients
Obstructions of the bile ducts, cholangitis, liver diseases, gallstones, active peptic ulcer and other biliary diseases.
Conditions where a reduced fluid intake is recommended (e.g. cardiac or renal disease).

4.4 **Special warnings and precautions for use**
Do not exceed the stated dose
If symptoms worsen or do not improve after one week or if symptoms such as fever, spasm, dysuria or blood in the urine occur, a doctor or qualified healthcare practitioner should be consulted.
The use in children and adolescents under 18 years of age is not recommended due to lack of adequate data. The use in the elderly is not relevant to the indication.
The use in patients with renal failure and/ or diabetes, and /or heart failure should be avoided because of possible risks due to hyperkalaemia.

Uva ursi leaf may cause a greenish-brown colouration of the urine.

Contains lactose monohydrate and sucrose. 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**
No interaction studies have been performed.
Additive effects with diuretics cannot be excluded and therefore concomitant treatment is not recommended.

4.6 **Fertility, 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.
Studies on the effects on fertility have not been performed.

4.7 **Effects on ability to drive and use machines**
No studies on the effects on the ability to drive or operate machines have been performed.

4.8 **Undesirable effects**
Nausea, vomiting, stomach ache have been reported with Uva ursi leaf.
Allergic reactions, epigastric pain and hyperacidity may occur with Dandelion Root. 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 cases of overdose 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.
Available tests on genotoxicity of Uva Ursi leaf are inadequate. Reproductive toxicity has not been studied. Available carcinogenicity studies have been negative. Arbutin, the principal component of Uva Ursi leaf, displayed some maternal and foetal toxicity in rats after subcutaneous administration of 400 mg/kg/day. No effect on reproduction has been observed at doses of 100 mg/kg/day.
Toxicity tests with hydroquinone, a hydrolysis product of arbutin, have demonstrated some evidence of genotoxicity and carcinogenicity. Risks posed by the exposure of hydroquinone during the short-term treatment with Uva Ursi leaf preparations are considered minimal.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Extract excipients
Maltodextrin
Colloidal anhydrous silica

Tablet core
Sucrose,
Lactose monohydrate.
Talc
Magnesium Stearate
Sodium Starch Glycolate
Cayenne

Tablet coat
Titanium Dioxide (E171)
Iron Oxide Black (E172)
Syrup

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store below 25ºC. Store in the original package

6.5 Nature and contents of container
Plastic container with tamper evident cap – 60 tablets.
Plastic container with tamper evident cap – 30 tablets

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

7 **MARKETING AUTHORISATION HOLDER**
Kerbina Limited
T/A Bio-Health Limited
Culpeper Close
Medway City Estate
Rochester
Kent
ME2 4HU

8 **MARKETING AUTHORISATION NUMBER(S)**
THR 00904/0002

9 **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
27/03/2013

10 **DATE OF REVISION OF THE TEXT**
27/03/2013
6 How to store this product

Do not use the tablets after the expiry date. The expiry date is printed on the pot label. The expiry date refers to the last day of that month. Return any unused tablets to your pharmacist who will dispose of them for you.

Store below 25°C in the original package.

Keep all medicines out of sight and reach of children.

Manufacturer and Traditional Herbal Registration Holder:
Karina Ltd T/A Bin-Health Ltd.
Culpeper House, Medway City Estate, Rochester, Kent ME2 4HU.

Traditional Herbal Registration number:
THR 00904/0002

Further information

Each coated tablet contains the following active herbal ingredients:
- 50mg of extract (as dry extract) from Bucho leaf
  (Agasthoma betulina (Bl.) Pillon) (4:1).
- 30mg of extract (as dry extract) from Uva Ursi leaf
  (Arctostaphylos uva-ursi (L.) Sprang) (2:6 - 4:5:1).
- 50mg of extract (as dry extract) from Dandelion root
  (Taraxacum officinale Weber ex Wigg) (3:5:1).

Each tablet also contains: Extract excipients: Matricaria recutita
Colloidal anhydrous silica. Tablet core: Sucrose, Lactose monohydrate,
Talc, Magnesium Stearate, Sodium Starch Glycolate, Cayenne.
Tablet coating: Titanium Dioxide (E171), Iron Oxide Black (E172), Syrup.

Each pot of Lowater contains either 30 or 60 tablets.

For large prints, Braille or audio version please contact +44 (0) 1634 390100.
This leaflet was revised in March 2013.
1 What Lownater Tablets are and what they are used for
A traditional herbal medicinal product used to relieve bloating associated with premenstrual water retention, based on traditional use only.

2 Before you take Lownater Tablets
Do not take if you:
- are allergic to any of the ingredients or plants of the Asteraceae (Compositae) family such as daisies, marigolds or artichokes (see section 6).
- are pregnant or breastfeeding.
- are under 18 years of age.
- have an obstruction, inflammation (cholecystitis) or disease of the bile ducts, gall stones, active peptic ulcer or other bile duct disease.
- have a condition where a reduced fluid is recommended such as heart or kidney disease.
- have diabetes.

The use in patients with renal failure and/or diabetes, and/or heart failure should be avoided because of possible side effects due to hyperkalemia.

Information about some of the ingredients
This product contains acacia and sucrose. Tell your doctor if you have an intolerance to some sugars.

Taking other medicines
Additive effects with diuretics cannot be excluded and therefore concomitant treatment is not recommended.

3 How to take Lownater Tablets

<table>
<thead>
<tr>
<th>Dosage</th>
<th>For oral short term use only, Swallow the tablets whole with water. Do not chew the tablets.</th>
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<tbody>
<tr>
<td></td>
<td>For adults: 2 tablets to be taken in the morning and 2 tablets in the evening. The tablets should be taken before the period is expected to start.</td>
</tr>
<tr>
<td></td>
<td>Do not exceed the recommended dose. The use in children and adolescents under 18 years of age and the elderly is not recommended.</td>
</tr>
<tr>
<td></td>
<td>If symptoms worsen or if fever occurs, spasm, painful urination or blood in the urine or symptoms persist for more than one week, consult your doctor or qualified healthcare practitioner.</td>
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</tbody>
</table>

4 Possible side effects
Nausea, vomiting and stomach ache have been reported with Uva ursi. The frequency is not known. Uva ursi may cause a granular brown discoloration of urine. Allergic reactions, stomach pain and sweats have been reported with delayed onset. The frequency is not known.

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

You can help to 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 from your GP's surgery or pharmacy, or call free phone 0800 731 6363, Yellow Card - 7am Monday - Friday.

MHRA PAR, LOWATER, THR 00904/0002
LABELLING

Labels:

LOWATER 30 TABLETS
Traditional herbal medicinal product used to relieve bloating associated with premenstrual water retention, based on traditional use only.

LOWATER 60 TABLETS
Traditional herbal medicinal product used to relieve bloating associated with premenstrual water retention, based on traditional use only.
Cartons: