

Peppermint Water BP 1973

THR 20346/0003

UKPAR

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PEPPERMINT WATER BP 1973

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Viridian Pharma Ltd a Traditional Herbal Registration certificate for the traditional herbal medicinal product Peppermint Water BP 1973 (Traditional Herbal Registration number: THR 20346/0003). This product is available without prescription and can be bought from pharmacies and other outlets.

The active ingredient of Peppermint Water BP 1973 is peppermint oil, which comes from the leaves of the peppermint plant, also known as *Mentha x piperita* L. Peppermint oil is a traditional herbal medicine used to relieve discomfort in the gut, such as indigestion, flatulence and stomach cramps. This registration is based exclusively upon the longstanding use of peppermint oil 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.

PEPPERMINT WATER BP 1973

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal remedy Peppermint Water BP 1973 (Traditional Herbal Registration number: THR 20346/0003) to Viridian Pharma Ltd on 23 June 2009. 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. This product is a traditional herbal medicinal product used for the symptomatic relief of minor digestive complaints such as dyspepsia, flatulence and stomach cramps, based on traditional use only.

The data supplied by the applicant demonstrate 30 years of traditional use of peppermint oil in the European Community. A satisfactory review of the available safety data on peppermint oil has also been provided, together with an expert report supporting the proposed product.

PHARMACEUTICAL ASSESSMENT

HERBAL SUBSTANCE: PEPPERMINT LEAF

Latin name: *Mentha x piperita* L.
Common name: Peppermint
Family: Lamiaceae
Parts of plant used: Leaf

No information has been provided on the herbal substance used to produce the peppermint oil (herbal preparation). This information is normally required for Herbal Medicinal Product application dossiers. However, in line with *CPMP/QWP/2819/00 rev 1 'Guideline on Quality of Herbal Medicinal Products / traditional Herbal Medicinal Products* where the herbal preparation is an essential oil or a fixed oil, the absence of the usual quality data relating to the herbal substance can be justified.

This applies, in particular, to essential and fixed oils which are items of international commerce and especially where they are widely used in the food/fragrance industries. In situations where the oil is the subject of a Ph Eur monograph (or national pharmacopoeia of a European Member State) and where the monograph is suitably comprehensive, the requirement for information on the herbal substance may be omitted.

In the case of the peppermint oil used in the current application, this is supplied by a major international supplier of essential oils. The peppermint oil monograph in the Ph Eur is considered to be state of the art and sufficient to control the herbal preparation. As the peppermint oil complies with the Ph Eur monograph it is considered acceptable as the active ingredient in the current product.

HERBAL PREPARATION: PEPPERMINT OIL

The peppermint oil is stated to comply with the Ph. Eur. and is a colourless, pale yellow or pale greenish-yellow liquid with a characteristic odour and taste.

Manufacture

A satisfactory description of the manufacturing process of the herbal preparation has been provided.

The in-process controls are satisfactorily detailed.

Satisfactory details of the 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.

The proposed specification has been justified satisfactorily and is in line with the Ph Eur monograph.

Container Closure System

The peppermint oil is stored in an appropriate container and Ph. Eur. conditions for storage are met.

Stability

Stability studies have been carried out on the herbal preparation. The results support the proposed retest period of 12 months following manufacture. This is acceptable.

HERBAL PRODUCT: PEPPERMINT WATER BP 1973

Description and Composition of the Herbal Product

The product is a clear and colourless oral solution containing peppermint oil, glycerol, nipasept sodium, (sodium methyl, ethyl and propyl parahydroxybenzoates [E219,E215 and E217]), carbomer, anhydrous citric acid and purified water. The glycerol, anhydrous citric acid and purified water are stated to comply with their respective Ph. Eur. monographs, the carbomer complies with its BP monograph. Nipasept sodium is controlled according to an appropriate in-house specification.

Manufacture

A description and flow-chart of the manufacturing method has been 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 packaged in 100 ml Amber Type III glass bottle with polypropylene screw cap with LDPE liner. Suitable specifications have been provided for the container closure system. The components of the primary packaging system also comply with Directive 2002/72 relating to contact with foodstuffs.

Stability

Finished product stability studies have been conducted under ICH conditions in accordance with current guidelines. Based on the results, a product shelf-life of 2 years with the storage precautions “Keep bottle in outer carton” and “Keep bottle tightly closed” is appropriate.

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.

NONCLINICAL ASSESSMENT

NONCLINICAL OVERVIEW

The applicant has submitted a good literature review with this application. The overview submitted in support of this application is satisfactory.

Due to a shortage of published data on peppermint, it is not possible to assess if the safety package for the peppermint 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.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

The SPC for this product is satisfactory from a preclinical 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

The information supplied demonstrates the traditional use of peppermint. An adequate literature review of peppermint has been carried out by the applicant and no new non-clinical data was submitted for assessment with this application. Granting of a THR is acceptable.

CLINICAL ASSESSMENT

PROPOSED INDICATION

The applicant has proposed the following:

“A traditional herbal medicinal product used for the symptomatic relief of minor digestive complaints such as dyspepsia, flatulence and stomach cramps, based on traditional use only.”

The indication is acceptable.

POSODOLOGY AND METHOD OF ADMINISTRATION

The applicant has proposed the following:

“Adults and the elderly

Two - eight 5 ml spoonfuls to be taken 3-4 times daily, as required

Children

Over 12 years of age – dose as for adults

Children of 12 years or younger – not recommended”

The posology is acceptable.

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 Community.

This application is for Peppermint Water as a herbal preparation. Peppermint Water has been used in the United Kingdom for the indication claimed for at least 30 years, as indicated by the monograph in Martindale The Extra Pharmacopoeia 26th Edition of 1972.

The information provided is fully satisfactory to demonstrate that the proposed product has been in use for at least 30 years of which at least 15 years have been in an EU Member State.

SAFETY REVIEW

Article 16 c 1 (D) requires the Applicant to provide bibliographic review of the safety data together with an expert report.

The information provided by the applicant was considered acceptable in view of the nature of the product and the fact that the active ingredient is Peppermint oil at low dosage.

A satisfactory review of the available safety data relating to peppermint oil has been provided together with an expert report supporting the registration of the product.

Product literature

The product literature (Summary of Product Characteristics, Patient Information Leaflet and labelling) for this product are medically 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.

DISCUSSION

This is an application for registration under the Traditional Herbal Medicinal Products Directive.

The data supplied by the Applicant are sufficient to demonstrate 30 years of traditional use within the European Community as required for registration under the Traditional Herbal Medicines Product Directive. A satisfactory review of the available safety data relating to peppermint has been provided together with an expert report supporting the registration of the product.

RECOMMENDATIONS

A Traditional Registration may be granted.

OVERALL CONCLUSION AND RISK ASSESSMENT

QUALITY

The quality data submitted with this application are satisfactory.

PRECLINICAL

No preclinical data were submitted and none are required for an application of this type.

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 ample evidence for the use of peppermint oil within the EU for a period exceeding 30 years.

The SPC, PIL and labelling are satisfactory.

RISK ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The risk: benefit ratio is, therefore, acceptable.

PEPPERMINT WATER BP 1973

THR 20346/0003

STEPS TAKEN FOR ASSESSMENT

- 1 The MHRA received the Traditional Herbal Registration application on 5 July 2007
- 2 Following standard checks and communication with the applicant the MHRA considered the application valid on 20 December 2007
- 3 Following assessment of the application the MHRA requested further information relating to the clinical dossier on 25 February 2008 and the quality dossier on 3 March 2008
- 4 The applicant responded to the MHRA's requests, providing further information on the clinical dossier on 5 September 2008 and the quality dossier on 22 October 2008
- 5 Following assessment of the response the MHRA requested further information relating to the quality dossier on 13 January 2009
- 6 The applicant responded to the MHRA's requests, providing further information on the quality dossier on 27 May 2009
- 7 A THR was granted on 23 June 2009

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Peppermint Water BP 1973

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml of oral solution contains 2.5 microlitres of Peppermint oil (*Mentha x piperita* L.)

Excipients:

Each 5 ml of oral solution contains 10 mg Nipasept Sodium, comprising; sodium methyl, ethyl and propyl parahydroxybenzoates.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral Solution

Clear and colourless

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

A traditional herbal medicinal product used for the symptomatic relief of minor digestive complaints such as dyspepsia, flatulence and stomach cramps, based on traditional use only.

4.2 Posology and method of administration

Adults and the elderly

Two - eight 5 ml spoonfuls to be taken 3-4 times daily, as required

Children

Over 12 years of age – dose as for adults

Children of 12 years or younger – not recommended

4.3 Contraindications

Hypersensitivity to Peppermint Oil preparations, menthol or any of the excipients. This product contains sodium methyl, ethyl, propyl parahydroxybenzoates [E219, E215 and E217]. If you are allergic to parahydroxybenzoates, do not take this product. Refer to Section 2 for content.

The product should not be used in patients with cholangitis, gallstones and any other biliary disorders that require medical supervision and advice.

4.4 Special warnings and precautions for use

Patients who already suffer from gastroesophageal reflux (heartburn) sometimes have an exacerbation of this symptom after taking peppermint oil. Treatment should be discontinued in these patients.

Peppermint oil should be used with caution with inflamed and ulcerated conditions of the gastrointestinal tract.

This product contains sodium methyl, ethyl, propyl parahydroxybenzoates [E219, E215 and E217] and should not be used by patients who are allergic to hydroxybenzoates. Allergic reactions may be delayed in onset.

Use in children under 12 years is not recommended as there is no experience available.

If symptoms worsen during the use of the product, a doctor or a qualified health care practitioner should be consulted.

4.5 Interaction with other medicinal products and other forms of interaction

None reported.

4.6 Pregnancy and lactation

Because data on the use of Peppermint Water during pregnancy and lactation are not available, its use is not recommended as a general precaution.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Contact sensitivity to menthol and peppermint oil in patients presenting with intra-oral symptoms in association with burning mouth syndrome, recurrent oral ulceration or a lichenoid reaction have been reported. The frequency is not known.

Allergic reactions to menthol have been reported, with headache, bradycardia, muscle tremor, ataxia, anaphylactic shock and erythematous skin rash. The frequency is not known.

If these or other adverse reactions not mentioned above occur, treatment should be discontinued and a doctor or a qualified healthcare professional consulted.

4.9 Overdose

No case of overdose has been reported with this product.

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**
Peppermint oil was negative in two validated tests of genotoxicity, the Ames test and the mouse lymphoma assay.

6 PHARMACEUTICAL PARTICULARS

- 6.1 List of excipients**
Glycerol
Nipasept Sodium, (sodium methyl, ethyl and propyl parahydroxybenzoates [E219,E215 and E217])
Carbomer
Citric Acid, anhydrous
Purified Water
- 6.2 Incompatibilities**
Not applicable
- 6.3 Shelf life**
2 years
- 6.4 Special precautions for storage**
Keep bottle in outer carton. Keep bottle tightly closed.
- 6.5 Nature and contents of container**
100 ml Amber Type III glass bottle with polypropylene screw cap with LDPE liner.
- 6.6 Special precautions for disposal**
No special requirements

7 MARKETING AUTHORISATION HOLDER

Viridian Pharma Ltd, Yew Tree House, Hendrew Lane, Llandevaud, Newport, Gwent NP18 2AB

8 MARKETING AUTHORISATION NUMBER(S)

THR 20346/0003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/06/2009

10 **DATE OF REVISION OF THE TEXT**
23/06/2009

PATIENT INFORMATION LEAFLET

Patient Information Leaflet

Peppermint Water BP 1973

Peppermint oil (*Mentha x piperita* L.)

Please read the entire leaflet carefully before you take this product.

- *Keep this leaflet. You may need to read it again.*
- *If you have further questions, please ask your doctor, pharmacist or qualified healthcare practitioner.*

In this leaflet:

1. What Peppermint Water BP 1973 is and what it is used for
2. Before you take Peppermint Water BP 1973
3. How to take Peppermint Water BP 1973
4. Possible side effects
5. How to store Peppermint Water BP 1973
6. Further information.

1. What Peppermint Water BP 1973 is and what it is used for

- Peppermint Water BP 1973 is a traditional herbal medicinal product containing 2.5 microlitres of Peppermint oil (*Mentha x piperita* L.) in each 5ml of oral solution.
- Peppermint Oil belongs to a group of products known as anti-flatulents
- This product is a traditional herbal medicinal product used to relieve discomfort in your gut, such as indigestion, flatulence and stomach cramps
This use is based on traditional use only

2. Before you take Peppermint Water BP 1973

Do not take this product if you :

- are allergic to any of the ingredients listed in this leaflet, or menthol, which is found in Peppermint Oil.
- are under 12 years old
- have gallstones or any disease of the bile ducts
- are suffering from heartburn, as it may make the heartburn worse.
- have an ulcer in your mouth, stomach or gut.

Pregnancy and breast-feeding
Peppermint Water BP 1973 is not recommended during pregnancy and lactation. You should consult your doctor, pharmacist or qualified healthcare practitioner if you are pregnant or breastfeeding.

Driving and using machines
No studies on the ability to drive and use machines have been performed.

Important information about some of the ingredients of Peppermint Water BP 1973
This product also contains sodium methyl, ethyl and propyl hydroxybenzoates (E219, E215 and E217) which may cause allergic reactions (possibly delayed)

3. How to take Peppermint Water BP 1973

Always shake the bottle thoroughly before use.

Peppermint Water BP 1973 is taken by mouth.

The dose can vary widely according to the level of your discomfort, but is normally:

Adults and the elderly:

Two - eight 5 ml spoonfuls to be taken 3-4 times daily, as required

Do not exceed the stated dose.

If you take too much of this product (overdose)

There are no reports of any adverse effects from taking too much but if you feel unwell talk to your doctor or qualified healthcare practitioner.

If you forget to take this product

Do not take a double dose. Take the next dose when it becomes due.

If you have any questions or are unsure about anything ask your doctor, pharmacist or qualified healthcare practitioner.

4. Possible side effects

Like all medicines Peppermint Water BP 1973 can cause side effects although not everybody gets them. There is a possibility you might develop hypersensitivity to menthol (which is found in Peppermint Oil) or Peppermint Oil itself. If you do you may suffer skin rash, headache, muscle tremor, effects

on heart rate, or other unexpected symptoms.

If you think you are having an allergic reaction to this product, or suspect any other side effect, tell your doctor, pharmacist or qualified healthcare practitioner as soon as you can.

5. How to store Peppermint Water BP 1973

Peppermint Water BP 1973 needs to be kept out of the reach and sight of children.

Keep bottle in outer carton. Keep bottle tightly closed.

Use by date: Do not use Peppermint Water BP 1973 after the expiry date on the label, or if there are any signs of discolouration or clouding of the solution.

6. Further information

What Peppermint Water BP* 1973 contains:

Each 10ml of oral solution contains 5 microlitres of the active substance Peppermint oil (*Mentha x piperita* L.)

Other ingredients are glycerol, carbomer, citric acid, sodium methyl,ethyl and propyl

hydroxybenzoates (E219,E215 and E217) and purified water
What this product looks like and content of the pack
Peppermint Water is a clear, sugar free liquid.

It is available in bottles of 100ml.

*BP stands for British Pharmacopoeia

Traditional Herbal Registration Holder

Viridian Pharma Ltd,
Yew Tree House,
Llandeudaud,
Newport, Gwent NP18 2AB
Telephone: 01633 400335

Manufacturer

Pharmacy Manufacturing Unit,
Queens Hospital,
Burton-on-Trent,
Staffs DE13 0RB

Traditional Herbal Registration No:
THR 20346/0003



This leaflet was approved: January 2009

LEAF0021/1



LABELLING

Label:

<p>Uses: a traditional herbal medicinal product used for the symptomatic relief of minor digestive complaints such as dyspepsia, flatulence and stomach cramps, based on traditional use only.</p> <p>Each 5ml contains: 2.5 microlitres of Peppermint Oil.</p> <p>Also contains: Sodium methyl, ethyl and propyl parahydroxybenzoates (E219, E215 and E217). See leaflet for further information.</p>	<p>PEPPERMINT WATER BP 1973</p> <p>Oral Solution</p> 	<p>Not recommended for children under 12 years old.</p> <p>Dose: Two - eight 5ml spoonfuls to be taken 3-4 times daily, as required.</p> <p>Shake bottle thoroughly before use.</p> <p>Do not exceed the stated dose.</p> <p>Keep bottle in outer carton. Keep bottle tightly closed. Keep out of the reach and sight of children.</p>  <p>Viridian Pharma Ltd Newport Gwent NP18 2AB THR 20346/0003</p>	<p>100ml</p>
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Carton:

