

# **SALVIAN Capsules**

**THR 15817/0005**

**UKPAR**

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## **SALVIAN CAPSULES**

**THR 15817/0005**

### **LAY SUMMARY**

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Bio-Health Limited a Traditional Herbal Registration Certificate for the traditional herbal medicinal product SALVIAN Capsules (Traditional Herbal Registration number: THR 15817/0005). This product is available without prescription and can be bought from pharmacies and other outlets.

SALVIAN Capsules are hypromellose capsules containing 300 mg of Sage leaf (*Salvia officinalis* L.). Sage leaf is a traditional herbal medicinal product used for the relief of excessive sweating associated with the menopause. This registration is based exclusively upon the longstanding use of Sage leaf 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.

**SALVIAN CAPSULES**

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**SCIENTIFIC DISCUSSION**

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## **INTRODUCTION**

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal remedy SALVIAN Capsules on 3 September 2009. This product is available without prescription and can be bought from pharmacies and other outlets.

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 data supplied by the Applicant demonstrate 30 years of traditional use of Sage leaf in the European Community. A satisfactory review of the available safety data on Sage leaf has also been provided, together with an Expert Safety Report supporting the proposed product.

## **PHARMACEUTICAL ASSESSMENT**

### **HERBAL SUBSTANCE: SALVIA LEAF**

**Scientific name of the plant:** *Salvia officinalis* L.

**Family:** Lamiaceae

**Synonyms of the herbal substance:** Sage

**Parts of the plant used:** leaf

### **Manufacture**

The plant source of the herbal substance Sage leaf is *Salvia officinalis* L., belonging to the Lamiaceae family. The plant material is collected from the wild in Albania in accordance with GACP guidelines without the use of pesticides and herbicides. The material is gathered during the flowering phase in summer in dry weather. The leaves are harvested and air dried and then stored at room temperature protected from direct sunlight.

The supplier of the Sage leaf has provided confirmation that the herbal substance is cultivated under GACP controlled conditions. Chemical treatments are not used on the wild collected plant material.

Assurance has been provided from the supplier that the Sage leaf has not been treated with fumigants (including ethylene oxide) or irradiation.

### **Control of Herbal Substance**

The starting material complies with the European Pharmacopoeia monograph. Certificates of analysis are presented for batches of the herbal drug giving full results for test parameters to support the proposed specification.

### **Container Closure System**

A suitable container closure system is used to store the herbal substance. The primary packaging materials comply with Directive 2002/72/EC.

### **Stability**

Information has not been provided, however, this is acceptable as the herbal substance is stored for a short period of time before encapsulation. Independent analysis is carried out to ensure compliance with European Pharmacopoeia specification.

## **HERBAL PRODUCT**

### **Description and Composition of the Herbal Product**

SALVIAN Capsules consist of hypromellose capsules, each containing 300 mg of powdered Sage Leaf.

Other than the hypromellose used to make the capsules, there are no excipients.

### **Manufacture**

A description and flow-chart of the manufacturing method has been provided. The manufacturing method is a standard procedure.

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.

#### **Finished product specification**

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. Certificates of analysis have been provided for any working standards used.

#### **Container Closure System**

The product is presented in HDPE plastic containers with a tamper evident threaded Duma cap. Either 30 or 60 capsules will be stored in these containers.

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 3 years with the storage precaution 'Store below 25°C in the original package' is appropriate.

#### **Pharmaceutical Expert**

The Quality Overall Summary has been written by a pharmacist with extensive experience with herbal products.

#### **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.

## **PRECLINICAL ASSESSMENT**

### **PRECLINICAL SAFETY DATA**

The Safety Expert Report submitted by the applicant lists relevant references to published work studying the acute toxicity, subacute toxicity and chronic toxicity of Sage leaf.

### **NONCLINICAL OVERVIEW**

The applicant has submitted an adequate literature review with this application. An Expert Safety Report was also provided, which included reviews of some nonclinical data. The Expert Safety Report was written by a medically qualified expert with suitable expertise in herbal medicines.

The Nonclinical Overview contains a short review of the nonclinical data for Sage leaf. Some of the studies in the literature review were conducted and published before GLP was a regulatory requirement. Moreover, it is not possible to ascertain if the data assessed in the review would comply with today's regulatory safety testing requirements with regards to design, conduct and analysis.

Due to a shortage of published data on Sage leaf it is not possible to assess if the safety package for the phytochemical constituents of Sage leaf meets current standards of 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/32116/0.

### **SUMMARY OF PRODUCT CHARACTERISTICS**

The Summary of Product Characteristic for this product is satisfactory.

### **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 demonstrating traditional use of Sage leaf is acceptable. An adequate literature review for Sage leaf has been carried out by the applicant and no new nonclinical data was submitted for assessment with this application. Granting of a THR is acceptable.

## **CLINICAL ASSESSMENT**

### **LEGAL STATUS**

General Sales List status is requested for the product. Sage is currently on the GSL Order.

### **PROPOSED INDICATION**

The applicant has proposed the following indication:

“A traditional herbal medicinal product used for the relief of excessive sweating associated with the menopause based on traditional use only”.

**Assessor’s comment:** The indication is acceptable and in line with HMPC Monograph for Sage leaf.

### **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.

The Applicant has provided a bibliographic review which shows evidence for the use of Sage leaf within the EU for a period exceeding 30 years.

### **SAFETY REVIEW**

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

The Applicant has provided satisfactory information supporting the safety of Sage leaf.

### **SUMMARY OF PRODUCT CHARACTERISTICS**

The SPC for this product is satisfactory.

### **PATIENT INFORMATION LEAFLET (PIL)**

The PIL for this product is satisfactory.

### **LABELLING**

All product labelling is satisfactory.

### **RECOMMENDATIONS**

A Traditional Registration may be granted.

## **OVERALL CONCLUSION AND RISK ASSESSMENT**

### **QUALITY**

The quality data submitted with this application is satisfactory.

### **PRECLINICAL**

No new 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 Sage leaf within the EU for a period exceeding 30 years.

A satisfactory review of the safety data has also been provided.

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.

## **SALVIAN CAPSULES**

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### **STEPS TAKEN FOR ASSESSMENT**

- 1 The MHRA received the Traditional Herbal Registration application on 18 March 2009
- 2 Following standard checks and communication with the applicant the MHRA considered the application valid on 01 April 2009
- 3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 28 April 2009
- 4 The applicant responded to the MHRA's requests, providing further information on the dossier on 11 June 2009
- 5 A THR was granted on 03 September 2009

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1 NAME OF THE MEDICINAL PRODUCT**

SALVIAN Capsules

### **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each capsule contains 300mg of Sage Leaf. (*Salvia officinalis L.*)  
For list of excipients see section 6.1.

### **3 PHARMACEUTICAL FORM**

Hard capsules.  
Clear size 0 hard capsules.

### **4 CLINICAL PARTICULARS**

#### **4.1 Therapeutic indications**

SALVIAN is a traditional herbal medicinal product used for the relief of excessive sweating associated with the menopause, based on traditional use only.

#### **4.2 Posology and method of administration**

For oral short term use only.  
Women experiencing menopausal symptoms:  
For the temporary relief of excessive sweating associated with the menopause.  
Take 1 capsule per day  
swallowed with water.  
Duration of use:- 2 weeks.  
If symptoms do not improve after 2 weeks during the use of SALVIAN a doctor or a qualified healthcare care practitioner should be consulted.  
There is no relevant use in children and adolescents under 18 years of age.

#### **4.3 Contraindications**

Patients with known hypersensitivity to Sage Leaf should not use SALVIAN.

#### **4.4 Special warnings and precautions for use**

There is no relevant use in children and adolescents under 18 years of age.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

None reported  
The intake of Sage preparations might influence the effect of medicinal products acting via GABA receptor (e.g. barbiturates, benzodiazepines), even if not seen clinically. Therefore the concomitant use with such medicinal products is not recommended.

#### **4.6 Pregnancy and lactation**

The safety of SALVIAN 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**

SALVIAN may impair ability to drive and use machines. Patients who are affected should not drive or operate machinery.

#### **4.8 Undesirable effects**

None Known.

If adverse reactions occur, a doctor or qualified health care practitioner should be consulted.

#### **4.9 Overdose**

Sage Leaf, at a dose in excess of 15g (equivalent to over 50 SALVIAN capsules), has been reported with a sense of heat, tachycardia, vertigo and epileptic form convulsions.

### **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**

Test on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

### **6 PHARMACEUTICAL PARTICULARS**

#### **6.1 List of excipients**

Hypromellose (capsule shell)

#### **6.2 Incompatibilities**

Not Applicable.

#### **6.3 Shelf life**

3 years.

#### **6.4 Special precautions for storage**

Store below 25°C in the original package.

- 6.5 Nature and contents of container**  
Duma 110ml HDPE plastic container and tamper evident threaded Duma cap.  
SALVIAN pack contains 30 or 60 Capsules.
- 6.6 Special precautions for disposal**  
There are no special precautions for disposal of SALVIAN capsules. When the container is empty the label should be removed and the container placed in a recycling bin.
- 7 MARKETING AUTHORISATION HOLDER**  
Bio-Health Limited  
Culpeper Close  
Medway City Estate  
Rochester  
Kent  
ME2 4HU
- 8 MARKETING AUTHORISATION NUMBER(S)**  
THR 15817/0005
- 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**  
03/09/2009
- 10 DATE OF REVISION OF THE TEXT**  
03/09/2009

## **PATIENT INFORMATION LEAFLET**

User Information Leaflet



# Salvian<sup>®</sup>

**SAGE LEAF 300mg  
30/60 CAPSULES**

**Please read this leaflet carefully before using Salvian.  
It contains important information about this medicine.**

**Keep this leaflet.**

You may want to read it again. If you need more information or advice, please ask your doctor, pharmacist or qualified health care practitioner.

**What is in this leaflet**

- |   |  |        |
|---|--|--------|
| 1 | What Salvian is and what it is used for          | Page 2 |
| 2 | Before you take Salvian                          | Page 2 |
| 3 | How to take Salvian                              | Page 2 |
| 4 | Side effects                                     | Page 3 |
| 5 | Further information on using and storing Salvian | Page 3 |
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### **1 What Salvia is and what it is used for**

Salvia is a traditional herbal medicinal product used for the relief of excessive sweating associated with the menopause, based on traditional use only.

### **2 Before you take Salvia**

Do not take if you:

- are allergic to the ingredient (see section 6).
- are pregnant or breastfeeding.
- are under 18 years of age.

Tell your doctor if you have an intolerance to any of the ingredients. This product may impair ability to drive and use machines, if affected do not drive or operate machines.

### **3 How to take Salvia**

#### **Dosage**

Swallow the capsules whole with water. Do not chew the capsules.

#### **Women experiencing menopausal symptoms:**

For the temporary relief of excessive sweating associated with the menopause: Take 1 capsule per day.

Duration of use:- 2 weeks.

**Do not exceed the recommended dose.**

**There is no relevant use in children and adolescents under 18 years of age.**

**If you take too much Salvian (overdose)**

If you take more than the recommended dose, see a doctor, pharmacist or qualified health care practitioner and take this leaflet with you.

**If you forget to take Salvian**

Continue to take your usual dose at the usual time; it does not matter if you have missed a dose.

**If you are unsure about anything relating to Salvian**

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

**4 Side effects**

There are no known side effects.

If you notice any other side effects after taking Salvian, please inform your **doctor** or **pharmacist**.

**5 Further information on using and storing Salvian**

If your symptoms of excessive sweating persists for more than four weeks after using this product, tell your doctor.

**Do not use the capsules after the expiry date.**

The expiry date is printed on the pot label. Return any unused capsules 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:

**Bio-Health Ltd.**

Culpeper Close,  
Medway City Estate,  
Rochester,  
Kent ME2 4HU.

**Traditional Herbal Registration number:**

THR 15817/0005



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## 6 Product Description

**Each hard capsule of Salvia contains the following active herbal ingredient:**

Sage Leaf 300mg (*Salvia officinalis* L.).  
There are no other ingredients in Salvia.



The capsule shell is made from hypromellose.

**Each pot of Salvia contains either 30 or 60 capsules.**

This leaflet was produced in April 2009.

## **LABELLING**

**Label:**

<p>5 026470 5555</p> <p>BARCODE TO BE CONFIRMED</p> <p>Expiry Date: Lot No:</p> <p>Salvian 30 capsules ID No. SAL.001</p>	 <p><b>Salvian<sup>®</sup></b></p> <p><b>SAGE LEAF 300mg 30 CAPSULES</b></p> <p>Traditional herbal medicinal product for the relief of excessive sweating associated with the menopause, based on traditional use only.</p>	<p><b>Do not purchase if seal is broken. Keep out of reach of children. Store below 25°C in the original package.</b></p> <p>Do not take during pregnancy or lactation. Not recommended for children or adolescents under 18 years of age.</p> <p><b>DOSAGE INSTRUCTIONS</b> Adults and elderly:</p> <p>For the relief of excess sweating associated with the menopause.</p> <p>Take 1 capsule per day, swallowed with water.</p> <p><b>Do not exceed the stated dose.</b></p>	<p><b>EACH HARD CAPSULE CONTAINS</b> Sage Leaf 300mg. (<i>Salvia officinalis</i> L.)</p> <p>Salvian is a traditional herbal medicinal product for the relief of excessive sweating associated with the menopause, based on traditional use only.</p> <p>Patients with known hypersensitivity to Sage Leaf should not use Salvian.</p> <p>If symptoms persist, or adverse reactions occur, consult a doctor or qualified healthcare practitioner.</p> <p>Traditional herbal registration holder/manufacture: <b>Bio-Health Ltd.,</b> Rochester England ME2 4HU THR 15817/0005</p> <p> <b>THR</b> Certification Mark</p>
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**Carton:**

