Holland & Barrett Black Cohosh Menopause Relief Tablets
GNC Live Well Black Cohosh Menopause Relief Tablets
Lifecycle Black Cohosh Menopause Relief Tablets
Nature’s Garden Black Cohosh Menopause Relief Tablets
Nature’s Bounty Black Cohosh Menopause Relief Tablet

THR 21710/0025

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted NBTY Europe Limited a Traditional Herbal Registration Certificate for the traditional herbal medicinal products Holland & Barrett Black Cohosh Menopause Relief Tablets, GNC Live Well Black Cohosh Menopause Relief Tablets, Lifecycle Black Cohosh Menopause Relief Tablets, Nature’s Garden Black Cohosh Menopause Relief Tablets and Nature’s Bounty Black Cohosh Menopause Relief Tablet (Traditional Herbal Registration number: THR 21710/0025) on 10 December 2014. These products are identical to each other apart from the difference in product name and will be collectively referred to as Menopause Relief Tablets in the remainder of this report. Menopause Relief Tablets are available without prescription and can be bought from pharmacies and other outlets.

The active ingredient in Menopause Relief Tablets comes from the rhizome and root of the Black Cohosh plant, which is also known as *Cimicifuga racemosa*. Menopause Relief Tablets is a traditional herbal medicinal product used for the relief of symptoms of the menopause, such as hot flushes, night sweats, and temporary changes in mood. This is based on traditional use only.

This registration is based exclusively upon the longstanding use of Black Cohosh rhizome and 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 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.
SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Menopause Relief Tablets (THR 21710/0025) to NBTY Europe Limited on 10 December 2014. 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. Menopause Relief Tablets is a traditional herbal medicinal product used for the relief of symptoms of the menopause, such as hot flushes, night sweats, and temporary changes in mood, based on traditional use only.

There is sufficient evidence to demonstrate use of Black Cohosh rhizome and root for at least 30 years, of which at least 15 years have been in an EU Member State. A satisfactory review of the available safety data on Black Cohosh rhizome and root has also been provided, together with an Expert Safety Report supporting the proposed product.
PHARMACEUTICAL ASSESSMENT

HERBAL SUBSTANCE: BLACK COHOSH RHIZOME AND ROOT

Scientific name of the plant: *Cimicifuga racemosa* (L) Nutt.
Plant family: Ranunculaceae

Manufacture of Herbal Substance
The herbal substance is cultivated in Europe and the USA.

The suppliers of the Black Cohosh rhizome and root provided confirmation that the herbal substance is produced in accordance with the principles of Good Agricultural and Collection Practice (GACP) (EMEA/HMPC/246816/20050).

Control of Herbal Substance
The herbal substance is controlled by a suitable specification.

Container Closure System
Satisfactory details of the container closure system are provided and confirmation has been given that all components of the container closure system comply with current legislation relating to plastic materials and articles intended to come into contact with foodstuffs.

Stability of Herbal Substance
Confirmation is given that the herbal substance will be tested immediately prior to being used to make the herbal preparation. A shelf-life for the herbal substance is not necessary because it is only a precursor of the active substance, the herbal preparation. The actual guideline requires stability testing data for the herbal preparation and the herbal product in the application documents and not for the herbal substance.

HERBAL PREPARATION: BLACK COHOSH RHIZOME AND ROOT DRY EXTRACT

Extract solvent: Ethanol 75% v/v
Drug extract ratio (native): 5-8:1

Manufacture of Herbal Preparation
A satisfactory description of the manufacturing process of the herbal preparation and flow diagram has been provided. The in-process controls are satisfactorily detailed. Certificates of Analysis for all 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 specifications.

**Container Closure System**
Satisfactory details of the container closure system are provided and confirmation has been given that all components of the container closure system comply with current legislation relating to plastic materials and articles intended to come into contact with foodstuffs.

**Stability of Herbal Preparation**
Stability studies have been carried out under ICH conditions. The results support the proposed retest period of the herbal preparation.

**HERBAL PRODUCT: MENOPAUSE RELIEF TABLETS**

**Description and Composition of Herbal Product**
Menopause Relief Tablets are speckled brown, round tablets that are plain on both sides. Each tablet contains 5mg of dry extract from Black Cohosh rhizome and root and the excipients maltodextrin and colloidal anhydrous silica (from the extract), microcrystalline cellulose, croscarmellose sodium, magnesium stearate and colloidal hydrated silica.

The compatibility of the herbal preparation with the excipients is demonstrated by the stability testing results. The excipients are controlled in line with their respective Ph Eur monographs and representative Certificates of Analysis are provided to demonstrate full compliance with the Ph Eur.

The magnesium stearate used in the product is confirmed to be of vegetable origin.

**Manufacture of Herbal Product**
A flow diagram outlining the various stages of the manufacturing process and the in-process controls is provided.

In-process controls are appropriate considering the nature of the products and the method of manufacture. Currently, process validation has not been carried out on commercial batches, however, as the manufacturer has committed to carry out process validation on commercial batches following an appropriate process validation protocol, this is acceptable.

**Control of Herbal Product**
The finished product specifications are 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 capsules are stored in green polyethylene terephthalate (PET) bottles with a chiffon green, polypropylene hinge cap with an inner seal liner designed to lift ‘n’ peel. The inner seal acts as a tamper evident seal under the cap and comprises of a polyester film, polymer adhesive layer, polyester tab, polyolefin foam, aluminium foil and sealable polyester film. The product is available in packs of 50 or 100 tablets.

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 of Herbal Product**
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a product shelf-life of 18 months is appropriate when the storage precautions ‘Do not store above 25° C’, ‘Keep in the original packaging’ and ‘Keep the bottle tightly closed’ are applied.

**Pharmaceutical Expert**
The Quality Overall Summary has been written by a chemist with suitable experience.

**Product Literature**
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.

**CONCLUSION**
There are no objections to granting of a Traditional Herbal Registration from a quality point of view.
NON-CLINICAL ASSESSMENT

NON-CLINICAL OVERVIEW
The applicant has submitted a literature review with this application. An Expert Safety Report was provided, which included reviews of some non-clinical data. The Expert Safety Report was written by a suitably qualified professional.

The overview submitted in support of this application is satisfactory.

Due to a shortage of published data on Black Cohosh rhizome and root it is not possible to assess if the safety package for the phytochemical constituents of this active ingredient 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.

In view of the absence of results of genotoxicity testing, the applicant has provided assurance that results will be provided before the renewal of the registration.

The Committee on Herbal Medicinal Products (HMPC) Community Monograph and assessment report for Black Cohosh rhizome and root adequately cover any non-clinical safety issues.

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The SmPC for this product is satisfactory from a non-clinical 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
There are no objections to granting of a Traditional Herbal Registration from a non-clinical point of view.
INDICATIONS
The submitted the following therapeutic indications:

“A traditional herbal medicinal product used for the relief of symptoms of the menopause, such as hot flushes, night sweats, and temporary changes in mood. This is based on traditional use only.”

These indications are acceptable.

POSOLOGY AND METHOD OF ADMINISTRATION
The applicant has submitted the following:

“For oral use only.

Take 1 tablet daily. The tablet should be taken at the same time of the day if possible (morning or evening) Swallow the tablet whole with water.”

This is acceptable.

Efficacy
No clinical efficacy data is required for registration of Traditional Herbal Medicinal Products.

Evidence of Traditional Use
Article 16 c 1 (c) requires the applicant to provide bibliographic or expert evidence showing 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 European Community.

The herbal preparation in the product under assessment is covered by the HMPC Community Monograph and the HMPC, in drafting the monograph, have accepted the traditional use of Black Cohosh rhizome and root.

The proposed dosage is within the range recommended by the HMPC Monograph and is acceptable.

The requirements of the Directive are, therefore, considered to be met.

Safety Review
Article 16 c 1 (d) requires the applicant to provide a bibliographic review of the safety data together with an Expert Safety Report.

The HMPC assessment report for Black Cohosh rhizome and root covers the bibliographic data available and the safety of Black Cohosh rhizome and root has been demonstrated. The SmPC is in line with the HMPC Monograph.

Product Literature
The SmPC, PIL and labelling for this product are medically satisfactory.
CONCLUSION
There are no objections to granting of a Traditional Herbal Registration from a clinical point of view.
OVERALL CONCLUSION AND RISK ASSESSMENT

QUALITY
The quality data submitted with this application are satisfactory.

NON-CLINICAL
No new non-clinical data were submitted with this application. However, assurance was provided that the results of genotoxicity testing will be provided before renewal of this registration. This is satisfactory.

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

There is sufficient evidence to demonstrate use of Black Cohosh rhizome and root for at least 30 years, of which at least 15 years have been in an EU Member State, and a satisfactory review of the safety data has been provided.

The SmPC, PILs and labelling are satisfactory.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. The risk: benefit balance is acceptable and a Traditional Herbal Registration may be granted.
HOLLAND & BARRETT BLACK COHOSH MENOPAUSE RELIEF TABLETS
GNC LIVE WELL BLACK COHOSH MENOPAUSE RELIEF TABLETS
LIFECYCLE BLACK COHOSH MENOPAUSE RELIEF TABLETS
NATURE’S GARDEN BLACK COHOSH MENOPAUSE RELIEF TABLETS
NATURE’S BOUNTY BLACK COHOSH MENOPAUSE RELIEF TABLET

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STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the Traditional Herbal Registration application on 14 June 2013
2. Following standard checks and communication with the applicant the MHRA considered the application valid on 16 July 2013
3. Following assessment of the application the MHRA requested further information relating to the clinical dossier on 1 November 2013 and the quality dossier on 20 December 2013.
4. The applicant responded to the MHRA’s request, providing further information on the clinical dossier on 4 November 2013 and the quality dossier on 28 March 2014 and 14 August 2014
5. A THR was granted on 10 December 2014
SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
PATIENT INFORMATION LEAFLETS

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
Holland & Barrett Black Cohosh Menopause Relief Tablets

Label:

Active ingredients: Each tablet contains 5mg of extract (as dry extract) from Black Cohosh rhizome and root (Cimicifuga racemosa L. (Rutaceae)) equivalent to 25mg of Black Cohosh rhizome and root. Extraction solvent: Ethanol 75% v/v.

Dosage: For oral use only. For women experiencing menopausal symptoms. Take 1 tablet daily. The tablet should be taken at the same time of the day if possible (morning or evening). Swallow the tablet whole with water.

Duration of use: If symptoms worsen or do not improve after 12 weeks of taking this product or if any of the side effects listed in the leaflet become serious or if side effects not listed occur, a Doctor, Pharmacist or a qualified Healthcare Practitioner should be consulted.

Warnings: DO NOT EXCEED THE STATED DOSE
Do not take this product if you are:
- Under 18 years of age
- Pregnant, breastfeeding or of childbearing potential, unless contraception is used
- Allergic to Black Cohosh or any of the ingredients in this product
- Suffering from, or have had liver or kidney problems

Do not take this product if you have or have ever had treatment for bowel cancer or any other hormone-dependent tumours. Please read the enclosed leaflet carefully before using this product.


Reference: NUTRITIONIST: NUTRITIONIST 21710/0025

MHRA PAR, BLACK COHOSH MENOPAUSE RELIEF TABLET, THR 21710/0025
GNC Live Well Black Cohosh Menopause Relief Tablets

Label:

Active Ingredients: Each tablet contains 5mg of extract (as dry extract) from Black Cohosh (Cimicifuga racemosa (L.) Nutt.) (equivalent to 25mg-40mg of Black Cohosh rhizome and root). Extracts solvent: Ethanol 75% v/v.

Dosage: For oral use only. For women experiencing menopausal symptoms. Take 1 tablet daily. The tablet should be taken at the same time of the day if possible (morning or evening). Swallow the tablet whole with water.

Duration of use: If symptoms worsen or do not improve after 12 weeks of taking this product or if any of the side effects listed in the leaflet become serious or if side effects not listed occur; or if menopause symptoms resolve or are relieved. Consult a Healthcare Practitioner should be consulted.

Warnings:
- Do not exceed the stated dose.
- Do not use during pregnancy or breastfeeding.
- Do not use if allergic to Black Cohosh or any of the ingredients in this product.
- Do not use if suffering from, or have had liver or kidney problems.
- Do not use if you have or have ever had treatment for breast cancer or any other hormone-dependent tumors. Please read the enclosed leaflet carefully before using this product.


GNC Live Well

50 TABLETS

MHRA PAR; BLACK COHOSH MENOPAUSE RELIEF TABLET, THR 21710/0025
Lifecycle Black Cohosh Menopause Relief Tablets

Label:
Nature’s Garden Black Cohosh Menopause Relief Tablets

Labels:

- **Active Ingredient:** Each tablet contains 5mg of extract (as dry extract) from Black Cohosh rhizome and root (Cimicifuga racemosa (L.) Nutt.) (equivalent to 25mg of Black Cohosh rhizome and root). Extraction solvent Ethanol 70% v/v.
- **Dosage:** For oral use only. For women experiencing menopausal symptoms, take 1 tablet daily. This tablet should be taken at the same time of the day if possible (morning or evening). Swallow the tablet whole with water.
- **Duration of Use:** If symptoms worsen or do not improve after 12 weeks of taking this product or if any of the side effects listed in the leaflet become serious or if side effects not listed occur, a Doctor, Pharmacist or a qualified Healthcare Practitioner should be consulted.
- **Warnings:**
  - Do not exceed the stated dose.
  - Do not take this product if you are:
    - Under 18 years of age.
    - Pregnant, breast feeding or of childbearing potential, unless contraception is used.
    - Keep to Black Cohosh or any of the excipients in this product.
    - Suffering from, or have had liver or kidney problems.
  - Do not take this product if you have or have ever had treatment for breast cancer or any other hormone-dependent tumours.
  - Please read the enclosed leaflet carefully before using this product.

THR 21710/0025
Registration Holder: NESTY Concepts Limited, Michael Ryder House, Turley Way, Nuneaton, Warwickshire CV10 7RA, United Kingdom
Nature’s Bounty Black Cohosh Menopause Relief Tablet

Label: