Solgar Celery Seed Capsules

THR 34104/0007

UKPAR

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SOLGAR CELERY SEED CAPSULES

THR 34104/0007

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Solgar UK Ltd a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Solgar Celery Seed Capsules (Traditional Herbal Registration number: THR 34104/0007) on 16 December 2011. Solgar Celery Seed Capsules are available without prescription and can be bought from pharmacies and other outlets.

Solgar Celery Seed Capsules is a traditional herbal medicinal product used for the relief of rheumatic aches and pains, based on traditional use only. The active ingredient in Solgar Celery Seed Capsules comes from the seeds of the celery plant (*Apium graveolens* L.)

This registration is based exclusively upon the longstanding use of Celery seed 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.
SOLGAR CELERY SEED CAPSULES

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Solgar Celery Seed Capsules (THR 34104/0007) to Solgar UK Ltd on 16 December 2011. 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. The product is used for the relief of rheumatic aches and pains, based on traditional use only.

The data supplied by the applicant demonstrate 30 years of traditional use of Celery seed in the European Community. A satisfactory review of the available safety data on Celery seed has also been provided, together with an Expert Safety Report supporting the proposed product.
PHARMACEUTICAL ASSESSMENT

HERBAL SUBSTANCE: CELERY SEED

Scientific name of the plant: *Apium graveolens* L.
Plant family: Umbelliferae

The Celery plants are cultivated in India, China and Europe and are harvested manually all year. Following harvesting, the herbal substance is cut, possibly cleaned and dried in the sun or by air.

The herbal substance is produced in line with the Guideline on Good Agricultural and Collection Practice (GACP) EMEA/HMPC/246816/2005.

Control of Herbal Substance
An appropriate specification based on the British Herbal Pharmacopoeial Monograph for Celery seed is applied and is acceptable. The specification is supported by the batch data provided.

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
Confirmation is given that the herbal substance will be tested prior to being used to make the herbal preparation. A shelf-life for the herbal substance is not appropriate 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: CELERY SEED DRY EXTRACT

Drug extract ratio (DER): 4-6:1
Extraction solvent: Ethanol 50 % (V/V)

Manufacture
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 batches of the herbal preparation, demonstrating satisfactory compliance with the proposed specification.

**Container Closure System**

Confirmation is provided that all components of the container closure system used to store the herbal preparation comply with current legislation relating to plastic materials and articles intended to come into contact with foodstuffs.

**Stability**

Stability studies have been performed in accordance with current guidelines. The proposed re-test period for the Celery seed dry extract is acceptable.

**HERBAL PRODUCT:** SOLGAR CELERY SEED CAPSULES

**Description and Composition of the Herbal Product**

Solgar Celery Seed Capsules are two-piece, clear, hard capsules with a light brown fill. Each capsule contains 112 mg of dry extract from Celery seed and the excipients maltodextrin and colloidal silica anhydrous (from the extract), microcrystalline cellulose, magnesium stearate and colloidal silica hydrated. The capsule shell is composed of hypromellose.

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 monograph 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 and, therefore, carries no TSE risk.

**Manufacture**

A flow diagram outlining the various stages of the manufacturing process and the in-process controls is provided. The manufacture of the herbal product is considered a standard procedure.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Currently, process validation has not been carried out on commercial batches, however, as the manufacturer has extensive experience and 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 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 capsules are stored in amber, glass, round bottles sealed with an inner liner made of paper backed aluminium. The bottles are covered with a gold-coloured metal screw cap. The product is available in packs of 30 capsules.

Suitable specifications have been provided by the packaging suppliers and it has been confirmed that all primary packaging materials comply with current requirements.

Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a product shelf-life of 24 months is appropriate when the storage precautions ‘Do not store above 25° C’, ‘Store in the original container’ and ‘Keep the container tightly closed’ are applied.

Pharmaceutical Expert
The Quality Overall Summary has been written by an expert with suitable experience.

Summary of Product Characteristics, labels 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.

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.

Due to a shortage of published data on Celery seed, it is not possible to assess if the safety package for the phytochemical constituents of these active ingredients 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.

Assurance was provided that the results of genotoxicity testing will be provided before renewal of the registration.

The overview submitted in support of this application is satisfactory.

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.
CLINICAL ASSESSMENT

INDICATION
The applicant has submitted the following therapeutic indication:

“A traditional herbal medicinal product used for the relief of rheumatic aches and pains, based on traditional use only.”

The indication is acceptable.

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

“For oral use only

Adults and the elderly
Take 1 capsule 3 times daily. Swallow the whole capsule with water.

Do not exceed the stated dose.

Duration of use:
If symptoms worsen or do not improve after 4 weeks, a doctor or a qualified healthcare practitioner should be consulted.

Not for use in children under 18 years of age (see section 4.4 Special warning and precautions for use)”

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 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 EU.

The applicant has provided a bibliographic review as evidence for the use of Celery seed within the European Community for a period exceeding 30 years.

The information provided is considered to satisfy the requirement to demonstrate use for at least 30 years, of which at least 15 years have been in an EU Member State. The requirements of the Directive are, therefore, addressed for this aspect.

SAFETY REVIEW
Article 16 c 1 (d) requires the applicant to provide a bibliography of the safety data together with an Expert Safety Report.
A safety review has been provided as well as an Expert Safety Report written by a suitably qualified professional. These are satisfactory.

**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. The applicant has provided a bibliographic review which shows evidence for the use of Celery seed within the EU for a period exceeding 30 years.

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

The SmPC, PIL and labelling are satisfactory.

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.
SOLGAR CELERY SEED CAPSULES

THR 34104/0007

STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the Traditional Herbal Registration application on 16 March 2011
2. Following standard checks and communication with the applicant the MHRA considered the application valid on 5 April 2011
3. Following assessment of the application the MHRA requested further information relating to the clinical dossier on 28 April 2011 and the quality dossier on 4 August 2011
4. The applicant responded to the MHRA’s requests, providing further information on the clinical dossier on 26 May 2011 and the quality dossier on 17 August 2011
5. A THR was granted on 16 December 2011
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Solgar Celery Seed Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule contains 112 mg of extract (as dry extract) from Celery Seed (Apium graveolens L.) (equivalent to 449 mg – 674 mg of Celery Seed). Extraction solvent: Ethanol 50% v/v.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Capsule, hard
Two piece clear hard capsules with light brown fill.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
A traditional herbal medicinal product used for the relief of rheumatic aches and pains, based on traditional use only.

4.2 Posology and method of administration
For oral use only

Adults and the elderly
Take 1 capsule 3 times daily. Swallow the whole capsule with water.

Do not exceed the stated dose.

Duration of use:
If symptoms worsen or do not improve after 4 weeks, a doctor or a qualified healthcare practitioner should be consulted.

Not for use in children under 18 years of age (see section 4.4 Special warning and precautions for use)

4.3 Contraindications
Hypersensitivity to celery seed, to plants of the Apiaceae (Umbelliferae) family or to carrots, mugwort, birch or dandelion.

Hypersensitivity to any of the excipients.

Patients with renal disease

Patients taking anti-coagulant medicines
4.4 **Special warnings and precautions for use**
- Do not exceed the stated dose
- If symptoms worsen or do not improve after 4 weeks, or if adverse effects not mentioned in the package leaflet occur, a doctor or a qualified healthcare practitioner should be consulted.
- If articular pain accompanied by swelling of joint, redness or fever are present a doctor should be consulted.
- The use in children and adolescents under 18 years of age is not recommended because data are not sufficient and medical advice should be sought.

In some cases, particularly in fair skinned individuals, sun burn type reactions on skin areas exposed to strong sunlight may occur due to photosensitisation by celery seed. Individuals using this product should avoid excessive sunbathing or the use of sunbeds or solariums.

4.5 **Interaction with other medicinal products and other forms of interaction**
None reported. However, there is a theoretical risk that Celery seed may interact with anti-coagulant medicines and should therefore not be used in patients receiving anti-coagulant medicines.

4.6 **Fertility, Pregnancy and lactation**
Safety during pregnancy and lactation has not been established. In the absence of sufficient data, use during pregnancy and lactation is not recommended. Studies on fertility have not been performed.

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**
- Allergic reaction in individuals sensitive to certain plants and species including wild carrots, mugwort, birch and dandelion
- Inflammation in individuals with renal disease.
- Skin inflammation and sensitivity to sunlight

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 case of overdose has 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**
Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

6 **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**
*Excipients in the extract:*
Maltodextrin
Colloidal silica anhydrous

*Excipients in the capsule:*
Microcrystalline cellulose
Magnesium stearate
Colloidal silica hydrated

*Capsule Shell:*
Hypromellose

6.2 **Incompatibilities**
Not applicable.

6.3 **Shelf life**
24 months

6.4 **Special precautions for storage**
Do not store above 25°C.
Store in the original container.
Keep the container tightly closed.

6.5 **Nature and contents of container**
*Container:* Amber glass, round bottle sealed with an inner liner made up of paper backed aluminium heat seal designed to seal glass bottles. The bottle is covered with a gold colour metal screw cap.

Pack size: 30 capsules

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

7 **MARKETING AUTHORISATION HOLDER**
Solgar UK Ltd
Beggars Lane
Aldbury
Tring
Hertfordshire
8 MARKETING AUTHORISATION NUMBER(S)
THR 34104/0007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
16/12/2011

10 DATE OF REVISION OF THE TEXT
16/12/2011
PATIENT INFORMATION LEAFLET

SOLGAR CELERY SEED CAPSULES
Celery Seed Extract 112 mg

IMPORTANT NOTES
• Please read this leaflet carefully before you use this product because it contains important information
• Keep this leaflet; you may need to read it again
• Seek professional advice if you need more information
• Please tell a doctor or a qualified healthcare practitioner if your symptoms worsen or do not improve
• Please tell a doctor or a qualified healthcare practitioner if you suffer from side effects not listed in this leaflet and/or if any of the side effects become serious

• Allergic to plants of the Apiaceae (Umbelliferae) family or to carrots, mugwort, birch or dandelion
• Taking medicines to thin the blood (anti-coagulants)

Some people, especially if fair-skinned, are more likely to develop sunburn-type reactions when taking Celery Seed products. As a result people using this product should avoid strong excessive sunbathing, sunbeds or solariums.

Consult a doctor or a qualified healthcare practitioner before taking Celery Seed if you are:
• Experiencing joint pain with any joint swelling or redness or a fever

3 - HOW TO TAKE THIS PRODUCT
For oral use only.
Adults and elderly:
Take 1 capsule 3 times daily.
Swallow the whole capsule with water.
Do not exceed the stated dose.

If you take too much of the product (overdose): Speak to a doctor or a qualified healthcare practitioner immediately and take this leaflet and bottle with you.

If you forget to take this product: Do not take a double dose to make up for the missed dose(s). Continue to take your usual dose at the usual time. It does not matter if you have missed a dose.

Duration of use: If symptoms worsen or do not improve after 4 weeks or if side effects not mentioned in this leaflet occur, a doctor or a qualified healthcare practitioner should be consulted.

IN THIS LEAFLET
1 What this product is and what it is used for
2 Before you take this product
3 How to take this product
4 Possible side effects
5 How to store this product
6 Further information

1 - WHAT THIS PRODUCT IS AND WHAT IT IS USED FOR
This product contains Celery Seed Extract. Solgar Celery Seed capsules is a traditional herbal medicinal product used for the relief of rheumatic aches and pains, based on traditional use only.

2 - BEFORE YOU TAKE THIS PRODUCT
Do not take this product if you are:
• Under 18 years of age
• Pregnant or breastfeeding
• Experiencing problems with kidney function
• Allergic to Celery Seed or any of the ingredients in this product (see section 6 of this leaflet)

Continued on back panel
4 - POSSIBLE SIDE EFFECTS
The following side effects can occur when using this product, although their frequency is not known:
- Allergic reaction in people who are sensitive to carrots, mugwort, birch or dandelion
- Inflammation in people who have kidney problems
- Skin inflammation and sensitivity to sunlight
If these symptoms persist for more than a few days or become troublesome, stop taking this product.
Stop taking this product immediately if you experience an allergic reaction.
If any of the above side effects becomes serious or if you experience any other side effects not listed above, consult your doctor or qualified healthcare practitioner.

5 - HOW TO STORE THIS PRODUCT
- Keep the capsules in the bottle until it is time to take them
- Do not take the capsules after the expiry date (see outer label). The expiry date refers to the last day of the month
- Do not store above 25°C
- Store in original container
- Keep container tightly closed
- Keep the capsules out of sight and reach of children

6 - FURTHER INFORMATION
Each hard capsule contains 112 mg of extract (as dry extract) from Celery Seed (Apium graveolens L.) (equivalent to 449 mg - 674 mg of Celery Seed).
Extraction solvent: Ethanol 50% v/v.
This product also contains the following inactive (excipient) ingredients:
- Microcrystalline cellulose, magnesium stearate and colloidal silica hydrated. Along with maltodextrin and colloidal silica anhydrous from the extract, and hypromellose from the capsule shell.
Each bottle contains 30 clear, two piece hard capsules with light brown fill.

After taking this product: You must speak to a doctor or a qualified healthcare practitioner if:
- Your symptoms get worse
- Your symptoms do not improve
- Side effects not listed in this leaflet occur

Traditional Registration Holder:
THR 34104/0007

Solgar UK Ltd
Beggars Lane
Aldbury, Tring
Hertfordshire, HP23 5PT
United Kingdom

Manufacturer of this product:
NBTY Europe
Vitality House
Sixth Avenue
Centrum 100
Burton-on-Trent
DE14 2WP
United Kingdom

If you would like further information about this product, please contact:

Solgar UK Ltd
Beggars Lane
Aldbury, Tring
Hertfordshire, HP23 5PT
United Kingdom

Is this leaflet hard to see or read?
Contact us on:
Telephone: +44 (0) 1442 890 355
Fax: +44 (0) 1442 890 366
Email: solgarinfo@solgar.com

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 form from your GP’s surgery or pharmacy, or call freephone 0808 100 3352

Last revision: October 2011
Solgar® is a registered trademark of Solgar UK Ltd.
LABELLING

Label:

SOLGAR
CELELY SEED  CAPSULES
Celery Seed Extract 112 mg

A traditional herbal medicinal product used for the relief of rheumatic aches and pains, based on traditional use only.

Active Ingredients: Each hard capsule contains 112 mg of extract (as dry extract) from Celery Seed (Apium graveolens L.) (equivalent to 440 mg - 674 mg of Celery Seed).
Extraction solvent: Ethanol 50%, w/v.

Dosage: For oral use only:
Adults and elderly: Take 1 capsule 3 times a day.
Swallow the whole capsule with water.

Directions for use: Read the enclosed leaflet carefully before use.

Duration of use: If symptoms worsen or do not improve after 8 weeks, a doctor or qualified healthcare practitioner should be consulted.

Read the enclosed leaflet carefully before use.

Storage: Do not store above 25°C.
Store in original container.
Keep container tightly closed.
Keep out of sight and reach of children.

DO NOT EXCEED THE STATED DOSE.

Registration holder: Solgar UK Ltd.
Regan's Lane, Aldershot, Hampshire, GU12 6PR, UK

SOLGAR® is a registered trademark of Solgar UK Ltd.
Carton:
Warnings:
Do not exceed the stated dose.

Do not use if you are:
- Under 18 years of age
- Pregnant or breast feeding
- Experiencing problems with kidney function
- Allergic to any of the ingredients
- Allergic to plants of the Apiaceae (carrot family) family, celery, aniseed, fennel, chick or dill
- Taking medication to thin the blood
Some people, especially those taking any one of these, are more likely to develop problems when taking Celery Seed.

Speak to your doctor or pharmacist before taking this product if you are:
- Experiencing joint pain with any joint swelling, or tendons, or a fever
- You must read the enclosed leaflet carefully before using this product.

Storage: Do not store above 25°C.
Store inoriginal container.
Keep container tightly closed.
Keep out of sight and reach of children.

Expiry Date: see bottom.

Active Ingredients: Each hard capsule contains 112 mg of extract (as dry extract) from Celery Seed (Apium graveolens L.) (equivalent to 400 mg - 674 mg of Celery Seed).
Extraction solvent: Ethanol 50% v/v.

Dosage: For use in adults only.
Take 1 capsule 3 times daily.
Swallow the whole capsule with water.

Directions for use: Read the enclosed leaflet carefully before use.

Duration of use: If symptoms worsen or do not improve after 4 weeks, a course of qualified healthcare professional should be consulted.

MHRA PAR; SOLGAR CELERY SEED CAPSULES, THR 34104/0007

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