# Solgar St. John’s Wort Capsules

THR 34104/0001

UKPAR

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The Medicines and Healthcare products Regulatory Agency (MHRA) granted Solgar UK Ltd a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Solgar St. John’s Wort Capsules (Traditional Herbal Registration number: THR 34104/0001) on 2 December 2011. This product is available without prescription and can be bought from pharmacies and other outlets.

Solgar St. John’s Wort Capsules is a traditional herbal medicinal product used to relieve the symptoms of slightly low mood and mild anxiety, based on traditional use only. The active ingredient in Solgar St. John’s Wort Capsules comes from the aerial parts of St John’s wort, which is also known as Hypericum perforatum L.

This registration is based exclusively upon evidence of traditional use of St John’s wort aerial parts 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.
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INTRODUCTION

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal medicine Solgar St. John’s Wort Capsules (THR 34104/0001) to Solgar UK Ltd on 2 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. Solgar St. John’s Wort Capsules are used to relieve the symptoms of slightly low mood and mild anxiety, based on traditional use only.

The data supplied by the applicant demonstrate 30 years of traditional use of St John’s wort aerial parts, including at least 15 years of use in the European Community. A satisfactory review of the available safety data on St John’s wort has also been provided, together with Expert Safety Reports supporting the proposed product.
PHARMACEUTICAL ASSESSMENT

HERBAL SUBSTANCE: ST JOHN’S WORT AERIAL PARTS

Latin name of plant: Hypericum perforatum L.
Plant family: Hypericaceae
Common name of plant: St John’s wort

St John’s wort is a perennial plant of 1-3 feet in uncultivated ground (woods, hedges, roadsides and meadows). The leaves are pale green, sessile and oblong with pellucid dots or oil glands. The flowers are bright yellow. The calyx and corolla are marked with black dots and lines with five pear-shaped petals. The plant blooms from June to August.

Manufacture of Herbal Substance
The plants are collected manually from the wild in Chile in July and August. Following collection, the plants are dried in the sun.

The plants are collected in accordance with Good Agricultural and Collection Practice (GACP) guidelines. It is also stated that the plants are not treated with chemicals or irradiation following collection.

Assurance has been provided that the herbal substance is collected from the wild in a sustainable manner.

Control of Herbal Substance
An appropriate specification based on the Ph Eur monograph for St John’s wort aerial parts 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 of Herbal Substance
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 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: ST JOHN’S WORT AERIAL PARTS DRY EXTRACT

Extraction solvent: Ethanol 60% (v/v)
Drug extract ratio (DER): 5-7:1
Excipients: Maltodextrin and colloidal silica anhydrous

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. The manufacture of the herbal preparation is considered a standard procedure. 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
Batches were packed in the final container closure system and stored under ICH conditions. The stability results support the proposed shelf life of the herbal preparation.

HERBAL PRODUCT: SOLGAR ST. JOHN’S WORT CAPSULES

Description and Composition of Herbal Product
Solgar St. John’s Wort Capsules are two-piece, clear, hard, capsules with a green brown powder fill. Each capsule contains 284 mg of extract (as dry extract) from St John’s wort aerial parts and the excipients maltodextrin and colloidal silica anhydrous (that are part of the herbal preparation), hypromellose (which forms the capsule shell), microcrystalline cellulose, magnesium stearate and colloidal silica hydrated.

The choice of excipients is based on experience and compatibility of the chosen excipients with the herbal preparation and is confirmed by stability testing. All excipients used comply with their respective Ph Eur monograph and satisfactory Certificates of Analysis are provided to demonstrate full compliance with the Ph Eur.
There are no excipients of human or animal origin used in the manufacture of the product. The supplier has provided confirmation that the magnesium stearate contained in this product is 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 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 up of paper backed aluminium heat seal designed to seal glass bottles. The bottles are covered with a gold colour 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 legislation.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a product shelf-life of 2 years is appropriate when the storage precautions ‘Do not store above 25° C’, ‘Keep in the original container’ and ‘Keep container tightly closed’ are applied.

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

**Summary of Product Characteristics, Labelling 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
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 who is a pharmacologist and medical herbalist.

Due to a shortage of published data on St John’s wort, 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.

The Committee on Herbal Medicinal Products (HMPC) Community Monograph and assessment report for St John’s wort adequately cover the non-clinical safety issues for St. John’s wort. In particular, a mutagenicity test carried out on an extract similar to that in the product under assessment is described and accepted in the HMPC Monograph. It is, therefore, considered that no further testing of the extract is required.

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 to relieve the symptoms of slightly low mood and mild anxiety, 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 2 times daily.

Swallow the capsule whole with water.

Not for use in children or adolescents under 18 years (see section 4.4 ‘Special Warnings and Precautions for use’).

Duration of use:
If symptoms worsen or do not improve after 6 weeks of using the medicinal product, a doctor or a qualified Healthcare Practitioner should be consulted.

Do not exceed stated dose.”

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 European Community.

The extract 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 the extract.

The proposed indication for this product is in line with the HMPC Monograph.

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 bibliography of the safety data together with an expert report.

A safety review has been provided as well as an Expert Safety Report written by a suitably qualified professional who is a pharmacologist and medical herbalist. The safety review and Expert Safety Report are satisfactory.

In addition, the published HMPC assessment report for St John’s wort and the monograph adopted by the HMPC adequately cover the clinical safety issues for St John’s wort.

**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, the published HMPC assessment report and Community Monograph for St John’s wort adopted by the HMPC adequately cover the non-clinical safety issues associated with St John’s wort.

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

The published HMPC assessment report and Community Monograph for St John’s wort adopted by the HMPC adequately cover the evidence for traditional use of the extract in the product under assessment for at least 30 years and the clinical safety issues associated with St John’s wort.

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 benefit: risk balance is acceptable and a Traditional Herbal Registration may be granted.
SOLGAR ST. JOHN’S WORT CAPSULES

THR 34104/0001

STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the Traditional Herbal Registration application on 15 July 2010.
2. Following standard checks and communication with the applicant the MHRA considered the application valid on 22 July 2010.
3. Following assessment of the application the MHRA requested further information relating to the quality dossier on 16 December 2010 and the clinical dossier on 18 March 2011.
4. The applicant responded to the MHRA’s requests, providing further information on the quality and clinical dossiers on 2 May 2011.
5. Following assessment of the response the MHRA requested further information relating to the quality dossier on 22 June 2011.
6. The applicant responded to the MHRA’s request, providing further information on the quality dossier on 18 July 2011.
7. A THR was granted on 2 December 2011.
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Solgar St. John’s Wort Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each hard capsule contains 284 mg of extract (as dry extract) from St. John’s Wort aerial parts (Hypericum perforatum L.) (equivalent to 1422 mg – 1991 mg of St. John’s Wort).
Extraction solvent: ethanol 60%v/v.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Capsule, hard.

Two piece clear hard capsules with green brown powder fill.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
A traditional herbal medicinal product used to relieve the symptoms of slightly low mood and mild anxiety, based on traditional use only.

4.2 Posology and method of administration
For oral use only.

Adults and the elderly- Take 1 capsule 2 times daily.

Swallow the capsule whole with water.

Not for use in children or adolescents under 18 years (see section 4.4 ‘Special Warnings and Precautions for use’).

Duration of use:
If symptoms worsen or do not improve after 6 weeks of using the medicinal product, a doctor or a qualified Healthcare Practitioner should be consulted.

Do not exceed stated dose.

4.3 Contraindications
• Hypersensitivity to St. John’s Wort or any of the excipients in this product
• This product should not be used in patients with known dermal photosensitivity or those undergoing phototherapy or any photodiagnostic procedures.
• This product should not be taken concomitantly with any of the medicines specified in section 4.5. This is because St. John’s Wort (Hypericum perforatum) has been shown to induce the cytochrome P450 isoenzymes CYP1A2, CYP2C19, CYP2C9 and CYP3A4 as well as the transport protein P-glycoprotein. This results in pharmacokinetic interaction with a large number of medicines including a possible decrease in the effectiveness of those medicines.

• Pharmacodynamic interactions have also been identified with antidepressants, particularly the SSRI antidepressants and the triptan group of medicines.

4.4 Special warnings and precautions for use

• Do not exceed stated dose

• The product should be discontinued at least 10 days prior to elective surgery due to the potential for interactions with medicinal products used during general and regional anaesthesia

• The use of this product is not recommended in children and adolescents under 18 years of age because data is not sufficient and medical advice should be sought

• If the condition worsens or if symptoms persist for more than 6 weeks a doctor or qualified healthcare practitioner should be consulted

• This product is intended for the relief of symptoms of slightly low mood and mild anxiety. Patients with signs and symptoms of depression should consult a doctor for appropriate treatment

• In very rare cases, particularly in fair-skinned individuals, sunburn type reactions may occur on skin areas exposed to strong sunlight due to photosensitisation by St. John’s Wort. Patients taking 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

InteractionSubstances in St. John’s Wort (Hypericum perforatum) have been shown to induce the cytochrome P450 isoenzymes CYP1A2, CYP2C19, CYP2C9 and CYP3A4 as well as the transport protein P-glycoprotein. This results in pharmacokinetic interactions with a large number of medicines leading to a potential decrease in the effectiveness of those medicines.

The concomitant use of ciclosporin, tacrolimus for systemic use, amprenavir, indinavir and other protease-inhibitors, irinotecan and warfarin is contraindicated.

Special care should be taken in case of concomitant use of all drug substances the metabolism of which is influenced by CYP1A2, CYP3A4, CYP2C9, CYP2C19 or P-glycoprotein (e.g. amitriptyline, fexofenadine, benzodiazepines, methadone, simvastatin, digoxin, finasteride), because a reduction of plasma concentrations is possible

Users of oral contraceptives taking St. John’s Wort (Hypericum perforatum) may experience intracyclic menstrual bleeding and the risk of contraception failure is increased.
Clinically significant pharmacodynamic interactions have also been identified with SSRI antidepressants, and the triptan group of medicines used to treat migraine. Due to the increased risk of undesirable effects associated with these interactions this product should not be used concomitantly with these types of medicines.

This product should not be taken concomitantly with the medicines included in the Table below due to the increased risk of undesirable effects associated with St. John’s Wort.

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<th>Co-administered drug</th>
<th>Interaction</th>
<th>Recommendations concerning co-administration</th>
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</thead>
<tbody>
<tr>
<td><strong>Anaesthetics/pre-operative medicines</strong></td>
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<tr>
<td>Fentany, propofol, sevoflurane, midazolam</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Based on the elimination half–life of hypericin and hyperforin this product should be discontinued at least 10 days prior to elective surgery.</td>
</tr>
<tr>
<td><strong>Analgesics</strong></td>
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<tr>
<td>Tramadol</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
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<tr>
<td><strong>Anti-arrhythmics</strong></td>
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<tr>
<td>Ivabradine</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><strong>Antibacterials</strong></td>
<td></td>
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<tr>
<td>Erythromycin, clarithromycin, telithromycin</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
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<tr>
<td><strong>Anticoagulants (blood thinning medicines)</strong></td>
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<tr>
<td>Warfarin, acenocoumarol</td>
<td>Reduced anticoagulant effect and need for increased dose</td>
<td>Do not take with this product</td>
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<tr>
<td><strong>Antidepressants</strong></td>
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</table>
### Co-administered drug

<table>
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<th>Co-administered drug</th>
<th>Interaction</th>
<th>Recommendations concerning co-administration</th>
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</thead>
<tbody>
<tr>
<td><strong>Tricyclics</strong> eg Amitriptyline, Clomipramine</td>
<td>Increased serotonergic effects with increased incidence of adverse reactions.</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><strong>MAOIs</strong> eg moclobemide</td>
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<tr>
<td><strong>SSRIs</strong> eg citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline</td>
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<tr>
<td><strong>Others</strong> eg duloxetine, venlafaxine</td>
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<tr>
<td><strong>Antiepileptics</strong></td>
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<tr>
<td>All drugs in this class including: Carbamazepine, phenobarbital, phenytoin, primidone, sodium valproate</td>
<td>Reduced blood levels with increased risk of frequency and severity of seizures.</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><strong>Antifungals</strong></td>
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<tr>
<td>Itraconazole, voriconazole</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><strong>Antimalarials</strong></td>
<td></td>
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</tr>
<tr>
<td>Artemether, lumefantrine</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
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<tr>
<td><strong>Anti-parkinsons</strong></td>
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<tr>
<td>Rasagiline</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
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<tr>
<td><strong>Antipsychotics</strong></td>
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<tr>
<td>Aripiprazole</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
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<tr>
<td><strong>Antivirals</strong></td>
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<tr>
<td><em>HIV protease inhibitors:</em> Amprenavir, atazanavir, darunavir, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, tipranavir,</td>
<td>Reduced blood levels with possible loss of HIV suppression</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><em>HIV non-nucleoside reverse transcriptase inhibitors:</em> efavirenz, nevirapine, delavirdine</td>
<td>Reduced blood levels with possible loss of HIV suppression</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><strong>Anxiolytics</strong></td>
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<tr>
<td>Co-administered drug</td>
<td>Interaction</td>
<td>Recommendations concerning co-administration</td>
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<td>----------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Buspirone</td>
<td>Increased serotonergic effects with increased incidence of adverse reactions</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td>Aprepitant</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td>Cardiac glycosides</td>
<td>Reduced blood levels and loss of control of heart rhythms or heart failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td>CNS Stimulants</td>
<td>Reduced blood levels and loss of control of heart rhythms or heart failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td>Cytotoxics</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td>Hormonal contraceptives</td>
<td>Reduced blood levels with risk of unintended pregnancy and breakthrough bleeding.</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td>Hormone Replacement Therapy</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td>Hormone antagonists</td>
<td></td>
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</table>
### Co-administered Drug Interaction Recommendations

<table>
<thead>
<tr>
<th>Co-administered Drug</th>
<th>Interaction</th>
<th>Recommendations concerning co-administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exemestane</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><strong>Diuretics</strong></td>
<td></td>
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<tr>
<td>Eplerenone</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
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<tr>
<td><strong>5HT agonists</strong></td>
<td></td>
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<tr>
<td>Almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan</td>
<td>Increased serotonergic effects with increased incidence of adverse reactions</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><strong>Immunosuppressants</strong></td>
<td></td>
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<tr>
<td>Ciclosporin, tacrolimus</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><strong>Lipid regulating drugs</strong></td>
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<tr>
<td>Simvastatin, atorvastatin</td>
<td>Reduced blood levels with risk of transplant rejection.</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><strong>Lithium</strong></td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><strong>Proton pump inhibitors</strong></td>
<td></td>
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<tr>
<td>Lansoprazole, omeprazole</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
<tr>
<td><strong>Theophylline</strong></td>
<td>Reduced blood levels and loss of control of asthma or chronic airflow limitation</td>
<td>Do not take with this product</td>
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<tr>
<td><strong>Thyroid hormones</strong></td>
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<tr>
<td>throxine</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
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<tr>
<td><strong>Oral hypoglycaemic drugs</strong></td>
<td></td>
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<tr>
<td>Gliclazide</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product</td>
</tr>
</tbody>
</table>

### 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 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 and use machines have been performed.

4.8 Undesirable effects
• Gastrointestinal disorders (e.g. dyspepsia, anorexia, nausea, diarrhoea, constipation), allergic skin reactions (e.g. rash, urticaria, pruritus) fatigue and restlessness may occur. The frequency is not known
• Fair-skinned individuals may react with intensified sunburn-like symptoms under intense sunlight or strong ultra-violet (UV) irradiation
• Other adverse reactions that have been reported include headaches, neuropathy, anxiety, dizziness and mania
• If other adverse reactions not mentioned above occur, a doctor, pharmacist or a qualified health care practitioner should be consulted.

4.9 Overdose
There is no data on human overdose with St. John’s Wort.

After the intake of up to 4.5g dry extract per day for 2 weeks and additionally 15g dry extract just before hospitalisation seizures and confusion have been reported.
Where a large overdose has occurred, phototoxic reactions may occur. The skin of the patient should be protected for 1-2 weeks from UV irradiation and sunlight. Outdoor activities should be restricted and clothes and/or sun block preparations used to protect the skin from sunlight. Symptomatic and supportive measures should be taken as appropriate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC amended.

5.2 Pharmacokinetic properties
Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC amended.

5.3 Preclinical safety data
Studies on acute toxicity and repeated dose toxicity did not show signs of toxic effects.

The weak positive results of an ethanolic extract in the AMES-test (salmonella typhimurium TA 98 and TA 100, with and without metabolic activation) could be assigned to quercetin and are irrelevant to human safety

No signs of mutagenicity have been detected in further in vitro and in vivo test systems.

Tests on reproductive toxicity revealed equivocal results. Test on the carcinogenic potential have not been performed.
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
2 years

6.4 Special precautions for storage
Do not store above 25°C.
Keep in the original container.
Keep 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
HP23 5PT
United Kingdom
8 MARKETING AUTHORISATION NUMBER(S)
   THR 34104/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
   AUTHORISATION
   02/12/2011

10 DATE OF REVISION OF THE TEXT
    02/12/2011
SOLGAR ST. JOHN’S WORT CAPSULES
St. John’s Wort Extract 284 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 after 6 weeks of taking this product.
- Please tell a doctor, pharmacist, or a qualified healthcare practitioner if you suffer from side effects not listed in this leaflet or if any of the side effects become serious.

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 St. John’s Wort extract. Solgar St. John’s Wort capsules is a traditional herbal medicinal product used to relieve the symptoms of slightly low mood and mild anxiety. This is based on traditional use only.

2. BEFORE YOU TAKE THIS PRODUCT

Do not take this product if you are:
- Under 18 years of age
- To undergo surgery in the next 10 days
- Allergic to any of the ingredients (see section 6 of this leaflet)
- Pregnant or breastfeeding
- Having UV light treatment (phototherapy) for any condition
- Exceptionally sensitive to sunlight on your skin (photosensitive)
- Suffering from depression

Symptoms of depression include feelings of helplessness and hopelessness, loss of interest in daily activities, changes in appetite or weight, changes in sleeping patterns or habits, loss of energy and difficulty in concentrating.

If your doctor has told you that you are suffering from depression do not use this product.

If you think you may be suffering from depression, tell your doctor before taking this product.
PATIENT INFORMATION LEAFLET

- Antimalarials: Arteether, lumefantrine
- Anti-Parkinson: Rasagiline
- Antipsychotics: Aripiprazole
- Anxiolytics: Buspiron
- Treatment of post-operative vomiting: Aprepitant
- Barbiturates: Butobarbital, phenobarbital
- CNS Stimulants: Methyl phenidate
- Hormone antagonists: Exemestane
- Diuretics: Eplerenone
- Proton pump inhibitors: Lansoprazole, omeprazole
- Bronchodilator: Theophylline
- Antidiabetic medicine: Gliclazide

While you are taking this product:
- Avoid excessive sunbathing or use of sunbeds/solariums (see section 4)
- Stop using it at least 10 days prior to undergoing any surgery

Driving and operating machinery:
In rare cases St. John’s Wort may make you feel dizzy or sleepy. If affected do not drive or operate machinery.

3 - HOW TO TAKE THIS PRODUCT

For oral use only.
For adults and elderly:
Take 1 capsule 2 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 6 weeks, or if any of the side effects become serious or if any side effects not mentioned in the leaflet occur, speak to a doctor or qualified healthcare practitioner.

4 - POSSIBLE SIDE EFFECTS

Like all medicines, this product can have side effects. The following side effects have been reported:
- Gastrointestinal disorders such as indigestion, loss of appetite, nausea, diarrhoea and constipation.
- Fatigue and restlessness.
- Allergic skin reactions such as rash, hives or itching of the skin. If you experience allergic skin reactions, stop taking the product and consult your doctor.
- Sunburn-like reactions on skin exposed to strong sunlight or strong ultra-violet (UV) irradiation e.g. solarium, particularly in fair-skinned individuals.
- Other side effects that have been reported include headaches, nerve pain or tingling, anxiety, dizziness and mania.

If any of the above side effects becomes serious or if other side effects not mentioned above occur, a doctor or healthcare practitioner should be consulted.

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 the original container
- Keep the container tightly closed
- Keep the capsules out of sight and reach of children

6 - FURTHER INFORMATION

About this product: Each hard capsule contains 284 mg of extract (as dry extract) from St. John’s Wort aerial parts (Hypericum perforatum L.) (equivalent to 1422 mg - 1901 mg of St. John’s Wort).
Extraction solvent: Ethanol 60% 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 capsules with green/brown powder.

Traditional Registration Holder:
THR 34104/0001

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: November 2011
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LABELLING

Label:

Active Ingredients: Each hard capsule contains 284 mg of extract (as dry extract) from St. John’s Wort aerial parts (Hypericum perforatum L.) (equivalent to 1422 mg - 5591 mg of St John’s Wort). Extraction solvent: Ethanol 60% v/v.

Dosage: For oral use only.

For adults and elderly:
Take 1 capsule 2 times daily.
Swallow the whole capsule with water.

Duration of Use: If symptoms worsen or do not improve after 6 weeks, or if any of the side effects become serious or if any side effects not mentioned in the leaflet occur, speak to a doctor or a qualified healthcare practitioner.

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

MFRA PAR; SOLGAR ST. JOHN’S WORT CAPSULES, THR 34104/0001
Carton: