Lamberts St John’s Wort Tablets

Nature’s Best St John’s Wort Tablets

THR 34425/0001

UKPAR

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LAMBERTS ST JOHN’S WORT TABLETS
NATURE’S BEST ST JOHN’S WORT TABLETS

THR 34425/0001

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Lamberts Healthcare Limited a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Lamberts St John’s Wort Tablets and Nature’s Best St John’s Wort Tablets (Traditional Herbal Registration number: THR 34425/0001) on 17 March 2011. Lamberts St John’s Wort Tablets and Nature’s Best St John’s Wort Tablets are identical to each other apart from the difference in product names and will be collectively referred to as St John’s Wort Tablets in the remainder of this report. This product is available without prescription and can be bought from pharmacies and other outlets.

St John’s Wort Tablets 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 of St John’s Wort Tablets comes from St John’s wort (Hypericum perforatum L.) aerial parts.

This registration is based exclusively upon the longstanding 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.
LAMBERTS ST JOHN’S WORT TABLETS
NATURE’S BEST ST JOHN’S WORT TABLETS

THR 34425/0001

SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal medicinal product St John’s Wort Tablets (THR 34425/0001) to Lamberts Healthcare Limited on 17 March 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 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, 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 an Expert Safety Report supporting the proposed product.
**PHARMACEUTICAL ASSESSMENT**

**HERBAL SUBSTANCE:** ST JOHN’S WORT  
Latin name: *Hypericum perforatum* L.  
Common name: St John’s Wort  
Parts of the plant used: Aerial parts

**Manufacture of Herbal Substance**  
The herbal substance is collected manually from the wild in Chile. The aerial parts are collected in July and August, during the plant’s flowering period. Following collection, the herbal substance is dried in the sun.

Confirmation has been provided that the herbal substance is produced in line with the Guideline on Good Agricultural and Collection Practice (GACP) EMEA/HMPC/246816/2005 and 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 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 Directive 2008/39/EC 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:** ST JOHN’S WORT DRY EXTRACT  
Extraction solvent: Ethanol 60% (v/v)  
Drug extract ratio (DER): 5-7:1  
Excipients: Maltodextrin and silica colloidal anhydrous

**Manufacture**  
A satisfactory description of the manufacturing processes of the herbal preparation 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
Satisfactory specifications with appropriate tests and limits have 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 Directive 2008/39/EC 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 results support the proposed shelf life of the herbal preparation.

HERBAL PRODUCT: ST JOHN’S WORT TABLETS

Description and Composition of the Herbal Product
St John’s Wort Tablets are brown, speckled, oval shaped and clear film-coated. Each tablet contains 370 mg of dry extract from St John’s wort aerial parts. The rest of the tablet is composed of maltodextrin and silica colloidal anhydrous (from the herbal preparation) and maltodextrin, microcrystalline cellulose, croscarmellose sodium, stearic acid, magnesium stearate and silica colloidal anhydrous (which form the tablet core). The tablet is coated in hypromellose and glycerol.

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

Manufacture
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. Details of the process validation carried out on pilot scale batches, along with a validation protocol for production scale batches and a commitment to carry out process validation on production scale batches are provided and are satisfactory.

Control of Herbal Product
The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where
appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification.

**Container Closure System**
The tablets are sealed into PVC/PVDC aluminium foil blister strips of 15 tablets that are inserted into a carton. Each carton contains 30, 60 or 90 tablets.

Suitable specifications have been provided by the packaging suppliers and it has been confirmed that all primary packaging materials comply with Directive 2008/39/EC relating to plastic materials and articles intended to come into contact with foodstuffs.

**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’ and ‘Store in the original package’ are applied.

**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.
NON-CLINICAL ASSESSMENT

NON-CLINICAL ASPECTS
The Expert Safety Report submitted by the applicant lists relevant references to published work studying the toxicology of St John’s wort aerial parts.

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 St John’s wort aerial parts, 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.

A mutagenicity test has been carried out on a similar extract to that in the product under assessment and is accepted in the monograph for St John’s wort adopted by the Committee on Herbal Medicinal Products (HMPC). Therefore, it is considered that no further testing of the extract is required.

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

PROPOSED 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 short term use only

Adults and the elderly: The recommended dosage is 1 tablet daily.

The tablet should be swallowed whole with a little water or other liquid. The tablets should not be chewed. This product is not recommended for children or adolescents under 18 years of age (See Section 4.4. Special Warnings and precautions for use)

If symptoms worsen during the use of the product or persist for more than 6 weeks, a doctor or a qualified healthcare practitioner should be consulted.”

This is acceptable.

EFFICACY
No clinical efficacy data is required for registration of Traditional Herbal Medicinal Products (THMP).

EVIDENCE OF TRADITIONAL USE
St John’s wort is generally accepted to have a tradition of use as an herbal medicine. 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 which shows evidence for the medicinal use of St John’s wort aerial parts for more than 30 years, including at least 15 years within the EU. Therefore, there is sufficient evidence of traditional use of this herbal preparation and a traditional herbal registration can be granted.

SAFETY REVIEW
Article 16 c 1 (d) requires the applicant to provide a bibliography of the safety data together with an expert report.
The HMPC assessment report for St John’s wort aerial parts covers the bibliographic data available and the safety of this herb has been demonstrated. The SmPC is in line with the HMPC monograph.

PRODUCT LITERATURE
The SmPC, PIL and labelling for this product is medically satisfactory.

RECOMMENDATIONS
A Traditional Herbal Registration may be granted.
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. A mutagenicity test has been carried out on a similar extract to that in the product under assessment and is accepted in the monograph adopted by the HMPC. Therefore, it is considered that no further testing of the extract is required.

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 St John’s wort aerial parts for a period exceeding 30 years, including at least 15 years within the EU.

The published HMPC assessment reports and community monographs for St John’s wort adopted by the HMPC adequately cover the non-clinical and 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 risk: benefit balance is acceptable and a Traditional Herbal Registration may be granted.
## STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the Traditional Herbal Registration application on 1 July 2009
2. Following standard checks and communication with the applicant the MHRA considered the application valid on 19 August 2009
3. Following assessment of the application the MHRA requested further information relating to the quality dossier on 19 November 2009 and the clinical dossier on 17 December 2009
4. The applicant responded to the MHRA’s request, providing further information on the quality dossier on 9 April 2010
5. Following assessment of the response the MHRA requested further information relating to the quality dossier on 15 June 2010
6. The applicant responded to the MHRA’s requests, providing further information on the quality dossier on 17 January 2011 and the clinical dossier on 25 January 2011
7. Following assessment of the response the MHRA requested further information relating to the clinical dossier on 31 January 2011 and the quality dossier on 1 February 2011
8. The applicant responded to the MHRA’s requests, providing further information on the quality dossier on 15 February 2011 and the clinical dossier on 22 February 2011
9. A THR was granted on 17 March 2011
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
- Lamberts St John’s Wort Tablets
- Nature’s Best St John’s Wort Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each film coated tablet contains 370 mg of extract (as dry extract) from St John’s Wort aerial parts \((Hypericum perforatum \text{ L.})\) (5-7:1) (equivalent to 1850mg – 2590mg of St John’s Wort.)
Extraction solvent: Ethanol 60% V/V

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film-coated tablets
Clear Coated Brown Speckled Oval Shaped Tablet.

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 short term use only

\textit{Adults and the elderly:} The recommended dosage is 1 tablet daily.

The tablet should be swallowed whole with a little water or other liquid. The tablets should not be chewed.
This product is not recommended for children or adolescents under 18 years of age (See Section 4.4. Special Warnings and precautions for use)

If symptoms worsen during the use of the product or persist for more than 6 weeks, a doctor or a qualified healthcare practitioner should be consulted.

4.3 Contraindications
Hypersensitivity to the active substance or any of the excipients.

Patients with known dermal photosensitivity or patients undergoing phototherapy or other photodiagnostic procedures.

This product should not be taken concomitantly with the medicines included in Section 4.5. This is because St John’s wort (\textit{Hypericum perforatum}) has been shown to induce the cytochrome P450 isoenzymes CYP1A2, CYP2C9,
CYP2C19 and CYP3A4 as well as transport protein P-glycoprotein. This results in pharmacokinetic interactions with a large number of medicines including leading to a possible decrease in the effectiveness of those medicines.

In addition, pharmacodynamic interactions have also been identified with antidepressants, particularly the SSRI antidepressants and with the triptan group of medicines.

4.4 Special warnings and precautions for use

Do not exceed the stated dose.

If the condition worsens during the use of the product or if symptoms persist for more than 6 weeks, consult a doctor or qualified healthcare practitioner.

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

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 persons, sun burn type reactions on skin areas exposed to strong sunlight may occur due to photosensitisation by St John’s wort. Persons using this product should avoid excessive sunbathing or the use of sunbeds or solariums.

This 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 (see Section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Substances in St John’s Wort (Hypericum perforatum) have been shown to induce the cytochrome P450 isoenzymes CYP1A2, CYP2C9, CYP2C19 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 concentration is possible.

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

<table>
<thead>
<tr>
<th>Co-Administered Drug</th>
<th>Interaction</th>
<th>Recommendations concerning co-administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaesthetics/pre-operative medicines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fentanyl, propofol, sevoflurane, midazolam</td>
<td>Reduced blood levels with risk of therapeutic failure.</td>
<td>Based on the elimination half-lives of hypericin and hyperforin this product should be discontinued at least 10 days prior to elective surgery.</td>
</tr>
</tbody>
</table>

| Anaesthetics | | |
| Tramadol | Reduced blood levels with risk of therapeutic failure. | Do not take with this product. |

| Antianginals | | |
| Ivabradine | Reduced blood levels with risk of therapeutic failure. | Do not take with this product. |

| Anti-arrhythmics | | |
| Amiodarone | Reduced blood levels with risk of therapeutic failure. | Do not take with this product. |

| Antibacterials | | |
| Erythromycin, clarithromycin, telithromycin | Reduced blood levels with risk of therapeutic failure. | Do not take with this product. |

<p>| Anticoagulants | | |
| Warfarin, acenocoumarol | Reduced anticoagulant effect and need for increased dose. | Do not take with this product. |</p>
<table>
<thead>
<tr>
<th>Class</th>
<th>Interaction</th>
<th>Caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclics eg.</td>
<td>Increased serotonergic effects with increased incidence of adverse reactions.</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>amitriptyline, clomipramine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAOIs eg.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>moclobemide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRIs eg.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>citalopram, escitalopram,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>fluoxetine, fluvoxamine,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>paroxetine, sertraline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others eg.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>duloxetine, venlafaxine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiepileptics</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>All drugs in this class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>including:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>carbamazepine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>phenobarbitone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>phenytoin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>primidone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sodium valproate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antifungals</td>
<td>Reduced blood levels with risk of therapeutic failure.</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>Itraconazole, voriconazole</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antimalarials</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>Artemether, lumefantrine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-parkinsons</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>Rasagiline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Reduced blood levels with risk of therapeutic failure</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antivirals</td>
<td>Reduced blood levels with possible loss of HIV</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>HIV protease inhibitors:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MHRA PAR; LAMBERTS ST JOHN’S WORT TABLETS/ NATURE’S BEST ST JOHN’S WORT TABLETS, THR 34425/0001**
<table>
<thead>
<tr>
<th><strong>HIV nonnucleoside reverse transcriptase inhibitors:</strong></th>
<th>suppression.</th>
</tr>
</thead>
<tbody>
<tr>
<td>efavirenz, nevirapine, delavirdine</td>
<td></td>
</tr>
</tbody>
</table>

### Anxiolytics

<table>
<thead>
<tr>
<th><strong>Buspirone</strong></th>
<th>Increased serotonergic effects with increased incidence of adverse reactions.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aprepitant</strong></td>
<td>Reduced blood levels with risk of therapeutic failure.</td>
</tr>
</tbody>
</table>

Do not take with this product.

### Barbiturates

<table>
<thead>
<tr>
<th><strong>Butobarbital, phenobarbital</strong></th>
<th>Reduced blood levels with risk of therapeutic failure.</th>
</tr>
</thead>
</table>

Do not take with this product.

### Calcium channel blockers

<table>
<thead>
<tr>
<th><strong>Amlodipine, nifedipine, verapamil, felodipine</strong></th>
<th>Reduced blood levels with risk of therapeutic failure.</th>
</tr>
</thead>
</table>

Do not take with this product.

### Cardiac glycosides

<table>
<thead>
<tr>
<th><strong>Digoxin</strong></th>
<th>Reduced blood levels and loss of control of heart rhythm or heart failure.</th>
</tr>
</thead>
</table>

Do not take with this product.

### CNS Stimulants
<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylphenidate</td>
<td>Reduced blood levels with risk of therapeutic 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>Irinotecan, dasatinib, erlotinib, imatinib, sorafenib, sunitinib, etoposide, mitotane</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>Oral contraceptives</td>
<td>Reduced blood levels with risk of therapeutic failure.</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>Emergency Hormonal Contraception</td>
<td>Reduced blood levels with risk of therapeutic failure.</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>Hormonal implants, injections</td>
<td>Reduced blood levels with risk of therapeutic failure.</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>Transdermal patches, creams etc.</td>
<td>Reduced blood levels with risk of therapeutic failure.</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>Intra-uterine devices with hormones</td>
<td>Reduced blood levels with risk of therapeutic failure.</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 Replacement Therapy: Oral</td>
<td>Reduced blood levels with risk of therapeutic failure.</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>Transdermal patches, gels, Vaginal rings</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>Reduced blood levels with risk of therapeutic failure.</td>
<td>Do not take with this product.</td>
</tr>
<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>Diuretics</td>
<td>Reduced blood levels with risk of therapeutic failure.</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>Eplerenone</td>
<td>Reduced blood levels with risk of therapeutic failure.</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>5HT agonists</td>
<td>Increased serotonergic effects with increased incidence of adverse reactions.</td>
<td>Do not take with this product.</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>--------------------------------</td>
</tr>
<tr>
<td>Almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan and zolmitriptan</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **Immunosuppressants**       |                                                                                  |                                |
|-------------------------------|--------------------------------------------------------------------------------|                                |
| Ciclosporin, tacrolimus       | Reduced blood levels with risk of transplant rejection.                         | Do not take with this product.  |

| **Lipid regulating drugs**   |                                                                                  |                                |
|-------------------------------|--------------------------------------------------------------------------------|                                |
| Simvastatin, atorvastatin     | Reduced blood levels with risk of therapeutic failure.                           | Do not take with this product.  |

| **Lithium**                  |                                                                                  |                                |
|-------------------------------|--------------------------------------------------------------------------------|                                |
|                               | Reduced blood levels with risk of therapeutic failure.                           | Do not take with this product.  |

| **Proton pump inhibitors**   |                                                                                  |                                |
|-------------------------------|--------------------------------------------------------------------------------|                                |
| Lansoprazole, omeprazole      | Reduced blood levels with risk of therapeutic failure.                           | Do not take with this product.  |

| **Theophylline**              |                                                                                  |                                |
|-------------------------------|--------------------------------------------------------------------------------|                                |
|                               | Reduced blood levels and loss of control of asthma or chronic airflow limitation. | Do not take with this product.  |

| **Thyroid hormones**         |                                                                                  |                                |
|-------------------------------|--------------------------------------------------------------------------------|                                |
| Thyroxine                     | Reduced blood levels with risk of therapeutic failure.                           | Do not take with this product.  |

| **Oral hypoglycaemic drugs** |                                                                                  |                                |
|-------------------------------|--------------------------------------------------------------------------------|                                |
| Gliclazide                    | Reduced blood levels with risk of therapeutic failure.                           | Do not take with this product.  |
4.6 Pregnancy and lactation
Safety of the product during pregnancy and lactation has not been established. In the absence of sufficient data the use in pregnancy and lactation is not recommended.

4.7 Effects on ability to drive and use machines
No adequate studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects
Gastrointestinal disorders including dyspepsia, anorexia, nausea, diarrhoea or constipation; allergic skin reactions such as rash, urticaria, pruritis; fatigue and restlessness have been reported. 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 healthcare practitioner should be consulted.

4.9 Overdose
No case of overdose has been reported.
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.

When 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
The active constituents of St. John’s wort have not been definitively established.
However, hypericin, pseudohypericin, hyperforin and the flavonoids are considered to play a role in its activity.

5.2 Pharmacokinetic properties
The active ingredients of St John’s wort can interact with other medicinal agents in two ways. Firstly, active ingredients in St John’s wort that themselves are metabolised in the liver by the CYP3A4 isoenzyme, increase (induce) the activity of this enzyme so that it accelerates the elimination of
other medicinal agents which are degraded by the same pathway. This leads to a consequent reduction in the plasma concentration and effectiveness of these other substances. Secondly, the active ingredients in St John’s wort, like other type SRI or SSRI medicinal agents with an antidepressant action, can raise the concentration of serotonin in certain parts of the central nervous system so that this neurotransmitter can sometimes reach toxic levels, particularly when drugs containing St John’s wort are combined with other antidepressants.

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 could be detected in further in-vitro and in-vivo test systems.

Tests on reproductive toxicity revealed equivocal results.

Tests on carcinogenic potential have not been performed.

Phototoxicity:
After oral application of dosages of 1800mg of an extract per day for 15 days the skin sensitivity against UVA was increased, and the minimum dose for pigmentations was significantly reduced. In the recommended dosage, no signs of phototoxicity are reported.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients in the extract
Maltodextrin
Silica colloidal anhydrous

Tablet Core
Maltodextrin
Microcrystalline cellulose
Croscarmellose Sodium
Stearic Acid
Magnesium Stearate
Silica Colloidal Anhydrous

Tablet Coating
Hypermellose
Glycerol

6.2 Incompatibilities
Not applicable
6.3 **Shelf life**
2 years

6.4 **Special precautions for storage**
Do not store above 25 °C. Store in the original package.

6.5 **Nature and contents of container**
Tablets are packed into PVC/PVDC aluminium foil blister strips of 15 tablets in the following pack size; 30, 60, 90 Tablets and packed into a Carton.

Not all pack sizes may be marketed

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

7 **MARKETING AUTHORISATION HOLDER**
Lamberts Healthcare Limited
1, Lamberts Road,
Tunbridge Wells
Kent
TN2 3EH

8 **MARKETING AUTHORISATION NUMBER(S)**
THR 34425/0001

9 **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
17/03/2011

10 **DATE OF REVISION OF THE TEXT**
17/03/2011
Patient Information Leaflet

Lamberts® St John’s Wort tablets
Please read this information carefully before you start taking these tablets. It contains some important information about this product. Keep this leaflet with the tablets. You may want to read it again or show it to your doctor, pharmacist or qualified healthcare practitioner.

What is 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 is a traditional herbal medicinal product containing St John’s Wort.

Lamberts® St John’s Wort 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:
- Your skin is exceptionally sensitive to sunlight (photosensitive)
- You are having light treatment (phototherapy) for any condition
- You are suffering from depression (see below)
- You are pregnant or breastfeeding
- You are allergic to any of the ingredients (see section 6)
- You are under the age of 18 years

Suffering from depression?
Symptoms of depression include feelings of helplessness and hopelessness, loss of interest in daily activities, appetite or weight changes, changes in sleep pattern, loss of energy and difficulty concentrating. If your doctor has told you that you are suffering from depression do not use this product. If you think that you may be suffering from depression you should tell your doctor before taking this product.

While you are taking this product:
- avoid excessive sunbathing or the use of sunbeds/ solariums
- 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 use machines.

Taking this product with other medicines
St John’s Wort can affect the way some medicines work and reduce their effectiveness. Medicines that can be affected by St John’s Wort include prescription medicines, and those that you may have bought without a prescription. Therefore it is important that you do not take St John’s Wort if you are using any of the medicines listed below.

- All medicines for depression/anxiety: Amitriptyline, clomipramine, moclobemide, citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, duloxetine, venlafaxine.
- All hormonal replacement therapy (HRT) treatments: HRT tablets, patches, gels, vaginal rings.
- All medicines for thinning the blood (anticoagulants): Warfarin, acenocoumarol.
- All medicines for epilepsy: Carbamazepine, phenobarbitone, phenytoin, primidone, sodium valproate.
- All immunosuppressant medicines: Ciclosporin, tacrolimus.
- All medicines for HIV infections: Amprenavir, atazanavir, darunavir, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, tipranavir, efavirenz, nevirapine, delavirdine.
- Some medicines for cholesterol: Simvastatin, atorvastatin.
- Some medicines for cancer: Irinotecan, dasatinib, erlotinib, imatinib, sorafenib, sunitinib, etoposide, mitotane.
- Some medicines for heart disease: Digoxin, ivabradine, amiodarone.
- Some medicines for migraines: Almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan.
- Some medicines for high blood pressure: Amlodipine, nifedipine, felodipine, verapamil.
- A medicine for regulating mood: Lithium.
- A thyroid hormone: Thyroxine.
St John’s Wort may also affect the following medicines. Therefore do not take this product with these medicines unless a doctor has said it is safe to do so:

- fentanyl, propofol, sevoflurane, and midazolam (anaesthetics/pre-operative medicines)
- tramadol (an analgesic)
- erythromycin, clarithromycin and telithromycin (antibiotics)
- itraconazole and voriconazole (antifungals)
- arteether and lumefantrine (antimalarials)
- rasagiline (an anti-Parkinson’s medicine)
- aripiprazole (an antipsychotic medicine)
- buspirone (an anxiolytic)
- aperient (used to treat post-operative vomiting)
- butobarbital and phenobarbital (barbiturates)
- methyl phenidate (a central nervous system or CNS stimulant)
- exemestane (a hormone antagonist)
- eplerenone (a diuretic)
- lansoprazole and omeprazole (proton pump inhibitors)
- theophylline (a bronchodilator)
- glimepiride (an antidiabetic medicine)

3. How to take this product

Adults and the elderly:
Take 1 tablet daily. Swallow the tablets whole with some water or other liquid. Do not chew the tablets.

Do not exceed the stated dose.

If you take too much of this product (overdose)
If you take more than the recommended dose, speak to a doctor, pharmacist or qualified healthcare practitioner and take this leaflet with you.

If you forget to take this product
Continue to take your usual dose at the usual time, it does not matter if you have missed a dose.

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

After taking this product
If your symptoms worsen, if they do not improve after 6 weeks, if side effects become serious or if you experience side effects not mentioned in this leaflet, you must consult your doctor, pharmacist 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.

Also sunburn-like reactions on skin exposed to strong sunlight or strong ultra-violet (UV) irradiation e.g. solarium have been reported, particularly in fair skinned individuals. Other side effects that have been reported include headaches, nerve pain or tingling, anxiety, dizziness and mania.

You must speak to a doctor or qualified healthcare practitioner if your symptoms worsen, if they do not improve after six weeks, or if any of the side effects become serious or if you notice any side effects not mentioned in the leaflet.

You can help to make medicines safer by reporting any side effects to the Yellow Card Scheme at www.yellowcard.gov.uk. Alternatively you can get a paper Yellow Card form from your GP’s surgery or pharmacy, or call free phone 0800 100 3352 (available 10am-2pm Monday- Friday).

5. How to store this product

Do not store above 25°C. Store in the original package. Keep the tablets out of the reach and sight of children. Keep your tablets in the blister pack until it is time to take them.

Do not use Lamberts® St John’s Wort tablets after the expiry date which is stated on the box and blister pack. The expiry date refers to the last day of that month. Return any out-of-date tablets to your pharmacist.

6. Further information

Each film-coated tablet contains 370mg of extract (as dry extract) from St John’s Wort aerial parts (Hypericum perforatum L.) (5-7:1) (equivalent to 1850mg-2590mg of St John’s Wort). Extraction Solvent: Ethanol 60% V/V.

This product also contains the following ingredients:

Excipients in the extract - Maltodextrin, Silica Colloidal Anhydrous.

Tablet Core - Maltodextrin, Microcrystalline Cellulose, Croscarmellose Sodium, Stearic Acid, Magnesium Stearate, Silica Colloidal Anhydrous.

Tablet Coating - Hypromellose, Glycerol.

The tablets are clear coated, brown speckled and oval shaped.

Each pack contains 30, 60 or 90 coated tablets.

Not all pack sizes may be marketed.

Traditional registration holder for this product:
Lamberts Healthcare Ltd., 1 Lamberts Road, Tunbridge Wells, Kent TN2 3EH.
Manufacturer of this product: Thompson & Capper Ltd, Hardwick Road, Astmoor, Runcorn, Cheshire WA7 1PH.
Traditional Herbal Registration Number: THR34425/0001

If you would like further information about this product or would like a large print, Braille or audio version of this leaflet please contact: Lamberts Healthcare Ltd., 1 Lamberts Road, Tunbridge Wells, Kent TN2 3EH. Tel: 01892 554312.

This leaflet was printed in March 2011. LK63
**Patient Information Leaflet**

**Nature’s Best St John’s Wort Tablets**

Please read this information carefully before you start taking these tablets. It contains some important information about this product. Keep this leaflet with the tablets. You may want to read it again or show it to your doctor, pharmacist or qualified healthcare practitioner.

1. WHAT THIS PRODUCT IS AND WHAT IT IS USED FOR

This product is a traditional herbal medicinal product containing St John’s Wort extract.

**Nature’s Best** St John’s Wort 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:

- Your skin is exceptionally sensitive to sunlight (photosensitive)
- You are having light treatment (phototherapy) for any condition
- You are suffering from depression (see below)
- You are pregnant or breastfeeding
- You are allergic to any of the ingredients (see section 6)
- You are under the age of 18 years

**Suffering from depression?**

Symptoms of depression include feelings of helplessness and hopelessness, loss of interest in daily activities, change in appetite, weight changes, changes in sleep pattern, loss of energy and difficulty concentrating. If your doctor has told you that you are suffering from depression do not use this product. If you think that you may be suffering from depression you should tell your doctor before taking this product.

While you are taking this product:

- Avoid excessive sunbathing or the use of sunbeds/solariums
- Stop using it at least 10 days prior to undergoing any surgery

Driving and operating machines

In rare cases St John’s Wort may make you feel dizzy or sleepy. It affected do not drive or use machines.

**TAKING THIS PRODUCT WITH OTHER MEDICINES**

St John’s Wort can affect the way some medicines work and reduce their effectiveness. Medicines that can be affected by St John’s Wort include prescription medicines, and those that you may have bought without a prescription. Therefore it is important that you do not take St John’s Wort if you are using any of the medicines listed below.

**All hormonal contraceptives:** The birth control "pill", emergency contraceptives, hormone implants, creams, patches, intra-uterine devices with hormones.

**All medicines for depression/anxiety:** Amitriptyline, clomipramine, moclobemide, citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, duloxetine, venlafaxine.

**All hormonal replacement therapy (HRT) treatments:** HRT tablets, patches, gels, vaginal rings.

**All medicines for thinning the blood (anticoagulants):** Warfarin, acenocoumarol.

**All medicines for epilepsy:** Carbamazepine, phenobarbitone, phenytoin, primidone, sodium valproate.

**All immunosuppressant medicines:** Ciclosporin, tacrolimus.

**All medicines for HIV infections:** Amprenavir, atazanavir, darunavir, fosamprenavir, indinavir, lopinavir, nef stavir, ritonavir, saquinavir, tipranavir, etavirrenz, nevirapine, delavirdine.

**Some medicines for cholesterol:** Simvastatin, atorvastatin.

**Some medicines for cancer:** Irinotecan, dasatinib, erlotinib, imatinib, sorafenib, sunitinib, etoposide, milotane.

**Some medicines for heart disease:** Digoxin, ivabradine, amiodarone.

**Some medicines for migraine:** Almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan.

**Some medicines for high blood pressure:** Amlodipine, nifedipine, telcappine, verapamil.

**A medicine for regulating mood:** Lithium.

**A thyroid hormone:** Thyroxine.

St John’s Wort may also affect the following medicines. Therefore do not take this product with these medicines unless a doctor has said it is safe to do so:

- Fentanyl, propofol, sevoflurane, and midazolam (anaesthetics/pre-operative medicines)
- Tramadol (an analgesic)
- Erythromycin, clarithromycin and tetracycline (antibiotics)
- Itraconazole and voriconazole (anti-fungals)
- Artemether and lumefantrine (anti-malarials)
- Rasagiline (an anti-Parkinson’s medicine)
- Cripiprazole (an antipsychotic medicine)
- Buspirone (an anxiolytic)
- Oprepipant (used to treat post-operative vomiting)
3. HOW TO TAKE THIS PRODUCT

Adults and the elderly
Take 1 tablet daily. Swallow the tablets whole with some water or other liquid. Do not chew the tablets.
Do not exceed the stated dose.
If you take too much of this product (overdose)
If you take more than the recommended dose, speak to a doctor, pharmacist or qualified healthcare practitioner and take this leaflet with you.
If you forget to take this product
Continue to take your usual dose at the usual time, it does not matter if you have missed a dose.
If you have any questions, or are unsure about anything, please ask your doctor, pharmacist or qualified healthcare practitioner.

AFTER TAKING THIS PRODUCT

If your symptoms worsen, if they do not improve after 6 weeks, if side effects become serious or if you experience side effects not mentioned in this leaflet, you must consult your doctor, pharmacist 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.
Also sunburn-like reactions on skin exposed to strong sunlight or strong ultra-violet (UV) irradiation e.g. solarium have been reported, particularly in fair skinned individuals. Other side effects that have been reported include headaches, nerve pain or tingling, anxiety, dizziness and mania.
You must speak to a doctor or qualified healthcare practitioner if your symptoms worsen, if they do not improve after six weeks, or if any of the side effects become serious or if you notice any side effects not mentioned in the leaflet.

5. HOW TO STORE THIS PRODUCT

Do not store above 25°C. Store in the original package.
Keep the tablets out of the reach and sight of children.
Keep your tablets in the blister pack until it is time to take them.
Do not use Nature's Best St John's Wort tablets after the expiry date which is stated on the box and blister pack. The expiry date refers to the last day of that month. Return any out-of-date tablets to your pharmacist.

6. FURTHER INFORMATION

Each film-coated tablet contains 370mg of extract (as dry extract) from St John's Wort aerial parts (Hypericum perforatum L.) (5:7:1) (equivalent to 1850mg - 2590mg of St John's Wort).
Extraction Solvent: Ethanol 60% V/V
This product also contains the following ingredients:
Excipients in the extract - Maltodextrin, Silica Colloidal Anhydrous.
Tablet Core - Maltodextrin, Microcrystalline Cellulose, Croscarmellose Sodium, Stearic Acid, Magnesium Stearate, Silica Colloidal Anhydrous.
Tablet Coating - Hypromellose, Glycerol, The tablets are clear coated, brown speckled and oval shaped.
Each pack contains 30, 60 or 90 coated tablets.
Not all pack sizes marketed.
Traditional Registration Holder for this product:
Lamberts Healthcare Ltd. 1 Lamberts Road, Tunbridge Wells, Kent TN2 3EH.
Manufacturer of this product:
Thompson & Capper Ltd. Hardwick Road, Astmoor, Runcorn, Cheshire WA7 1PH.
Traditional Herbal Registration Number:
THR 34425/0001
If you would like further information about this product or would like a large print, Braille or audio version of this leaflet please contact:
Telephone: 01892 552 117
Email: info@naturesbest.co.uk
You can help to make medicines safer by reporting any side effects to the Yellow Card Scheme at www.yellowcard.gov.uk. Alternatively you can get a paper Yellow Card form from your GP's surgery or pharmacy, or call free phone 0800 100 3352 (available 10am - 2pm Monday – Friday).

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LABELLING

Blister:
Carton:
Blister:
Carton: