SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

UCalm St John's Wort Tablets
Care St John's Wort Low Mood Relief Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

300mg of extract (as dry extract) from St John's Wort aerial parts (*Hypericum perforatum* L.) (5-7:1) (equivalent to 1500 – 2100mg of St John's Wort).

Extraction Solvent: Ethanol 60%v/v.

Excipients: for full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets.

Round, dark brown shallow convex tablets

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.

For adults and the elderly, take 2 tablets once daily. The tablets should be swallowed whole with a little liquid. The tablets should not be chewed

This-product is not recommended for use in children or adolescents under 18 years (See section 4.4 'Special warnings and precautions for use')

A doctor or qualified healthcare practitioner should be consulted if symptoms worsen or do not improve after 6 weeks.

4.3 Contraindications

Hypersensitivity to the active ingredient or any of the excipients.

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

Concomitant use with ciclosporin, tacrolimus for systemic use, amprenavir, indinavir and other protease inhibitors, irinotecan and warfarin (see section 4.5 'Interactions with other medicinal products and other forms of interaction'). 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 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, or if symptoms persist for more than six weeks medical advice should be sought.

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 relief of symptoms of slightly low mood and mild anxiety. Patients with signs and symptoms of depression should seek medical advice 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 sun-beds 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, CYP2C19, CYP2C9 and CYP3A4 as well as 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 SSRI antidepressants, and the triptan group of medicines used to treat migraines. Due to 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 the table below.

Co-administered drug	**Interaction**	**Recommendations concerning co-administration.**
Anaesthetics / pre-operative medicines		
Fentanyl, Propofol Sevoflurane Midazolam	Reduced blood levels with risk of therapeutic failure	Based on the elimination half lives of hypericin and hyperforin, this product should be discontinued at least 10 days prior to elective surgery
Analgesics		
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.
Anticoagulants		
Warfarin	Reduced anticoagulant	Do not take with this

Acenocoumarol	effect and need for increased dose.	product.
Antidepressants		
Tricyclics eg Amitriptyline Clomipramine **MAOI's eg** Moclobemide **SSRI's eg** Citalopram Escitalopram Fluoxetine Fluvoxamine Paroxetine Sertraline **Others eg** Duloxetine Venlafaxine	Increased serotonergic effects with increased incidence of adverse reactions.	Do not take with this product.
Antiepileptics		
All drugs in this class including: Carbamazepine Phenobarbitone Phenytoin Primidone Sodium valproate	Reduced blood levels with increased risk of frequency and severity of seizures	Do not take with this product.
Antifungals		
Itraconazole Voriconazole	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
Antimalarials		
Artemether Lumefantrine	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
Anti-parkinsons		
Rasagiline	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
Antipsychotics		
Aripiprazole	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
Antivirals		
HIV protease inhibitors:	Reduced blood levels with possible loss of HIV	Do not take with this product.

Amprenavir Atazanavir, Darunavir, Fosamprenavir, Indinavir, Lopinavir, Nelfinavir, Ritonavir, Saquinavir, Tipranavir	suppression.	
HIV non-nucleoside reverse transcriptase inhibitors: Efavirenz, Nevirapine, Delavirdine	Reduced blood levels with possible loss of HIV suppression.	Do not take with this product.
Anxiolytics		
Buspirone	Increased serotonergic effects with increased incidence of adverse reactions	Do not take with this product.
Aprepitant	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
Barbiturates		
Butobarbital Phenobarbital	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
Calcium channel blockers		
Amlodipine, Nifedipine, Verapamil, Felodipine	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
Cardiac glycosides		
Digoxin	Reduced blood levels and loss of control of heart rhythm or heart failure.	Do not take with this product.
CNS Stimulants		
Methylphenidate	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
Cytotoxics		
Irinotecan, Dasatinib, Erlotinib, Imatinib, Sorafenib, Sunitinib, Etoposide, Mitotane	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
Hormonal contraceptives		
Oral contraceptives Emergency hormonal contraception Hormonal implants, injections.	Reduced blood levels with risk of unintended pregnancy and breakthrough bleeding.	Do not take with this product.

Transdermal patches, creams etc. Intra-uterine devices with hormones.		
Hormone Replacement Therapy		
Hormone Replacement Therapy: Oral Transdermal patches Gels Vaginal rings	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
Hormone antagonists		
Exemestane	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
Diuretics		
Eplerenone	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
5HT agonists		
Almotriptan, Eletriptan, Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan, and Zolmitriptan	Increased serotonergic effects with increased risk of adverse reactions	Do not take with this product.
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 Fertility, pregnancy and lactation

Safety of the product during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

No studies on the effects on fertility have been performed.

4.7 Effects on ability to drive and use machines

No studies 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 or qualified healthcare practitioner should be consulted.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' in the Google Play or Apple App Store.

4.9 Overdose

Symptomatic and supportive measures should be taken as appropriate.

After intake or 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. After ingestion of massive overdoses, the patient should be protected from sunlight and other UV-light sources for 1 -2 weeks. Outdoor activities should be restricted and clothes and/or sun block preparations used to protect the skin from sunlight.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other antidepressants

ATC code: N06AX

5.2 Pharmacokinetic properties

The absorption of hypericin is delayed and starts about 2 hours after administration. The elimination half-life is about 20 hours, the mean residence time about 30 hours. Maximum hyperforin levels are reached about 3 – 4 hours after administration: no accumulation could be detected. Hyperforin and the flavonoid miquelianin can cross the blood brain barrier Hyperforin induces the activity of the metabolic enzymes CYP3A4, CYP2C9, CYP2C19, and PGP dose-dependently via activation of the PXR system Therefore the elimination of other drug substances may be accelerated, resulting in decreased plasma concentrations.

The active ingredients in St John's Wort, like other type SRI or SRRI 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 per day for 15 days, the skin sensitivity against UVA was increased and the minimum dose for pigmentation was significantly reduced. In the recommended dosage, no signs of phototoxicity are reported.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Herbal extract:

Maltodextrin
Silica colloidal anhydrous

Tablet core:

Calcium hydrogen phosphate dihydrate
Cellulose microcrystalline
Hydroxypropylmethyl cellulose
Croscarmellose sodium
Silica colloidal hydrated
Magnesium stearate

Coating:

Sodium Carboxymethlycellulose
Lecithin
Dextrose monohydrate
Sodium citrate
Dextrin

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25^0C.

Store in the original packaging to protect from light and moisture.

6.5 Nature and contents of container

Amber glass bottle with polypropylene cap incorporating induction heat seal closure.
Printed outer carton containing Patient Information Leaflet.

Pack sizes of 30, 60, 90 and 120 tablets. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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