

SUMMARY OF PRODUCT CHARACTERISTICS

HYPERIFORCE ST. JOHN'S WORT TABLETS

1 NAME OF THE MEDICINAL PRODUCT

Hyperiforce St. John's wort tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains 40-73 mg of extract (as dry extract) from fresh St John's wort (*Hypericum perforatum* L.) flowering herb (3.1-4.0:1).

Extraction solvent: Ethanol 68% V/V.

One tablet contains 5.5 mg soya polysaccharide.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

It is a brownish, biconvex, bevelled 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.

Adults and the elderly: Take one tablet three times a day.

The patient should consult a doctor if symptoms worsen or do not improve after 6 weeks.

Children and adolescents less than 18 years old: This product is not indicated in patients less than 18 years.

4.3 Contraindications

Hypersensitivity to the active ingredient or any of the excipients.

This product contains soya polysaccharide. If you are allergic to peanut or soya, do not take this product. Refer to Section 2, Qualitative and Quantitative Composition for soya content.

The product should not be used in children or adolescents under 18 years of age.

Pregnancy and lactation (see Section 4.6).

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

This product should not be taken concomitantly with the medicines included in Section 4.5. This is because St John's wort (*Hypericum perforatum*) has been shown to induce the cytochrome P450 isoenzymes CYP1A2, 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 recommended dose.

If symptoms worsen or do not improve after six weeks medical advice should be sought.

The dosing and safety of St John's wort have not been studied in children/adolescents below 18 years and safety is not established.

This product contains soya oil polysaccharide and should not be used by patients who are allergic to peanut or soya.

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 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 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. Clinically significant interactions have been reported with for

example: warfarin, ciclosporin, HIV protease inhibitors, theophylline, digoxin, oral contraceptives, and anticonvulsants.

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:

Co-administered drug	Interaction	Recommendations concerning co-administration
<i>Anaesthetics / Pre-operative Medicines</i>		
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.
<i>Analgesics</i>		
Tramadol	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
<i>Antianginals</i>		
Ivabradine	Reduced blood levels with risk of therapeutic failure	Do not take with this product.
<i>Anti-arrhythmics</i>		
Amiodarone	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Antibacterials</i>		
Erythromycin, Clarithromycin, Telithromycin	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Anticoagulants</i>		
Warfarin, Acenocoumarol	Reduced anticoagulant effect and need for increased dose	Do not take with this product.
<i>Antidepressants</i>		

Tricyclics e.g. Amitriptyline, Clomipramine MAOIs e.g. Moclobemide SSRIs e.g. Citalopram, Escitalopram, Fluoxetine, Fluvoxamine, Paroxetine, Sertraline Others e.g. Duloxetine, Venlafaxine	Increased serotonergic effects with increased incidence of adverse reactions.	Do not take with this product.
<i>Antiepileptics</i>		
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.
<i>Antifungals</i>		
Itraconazole, Voriconazole	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Antimalarials</i>		
Artemether, Lumefantrine	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Antiparkinsons</i>		
Rasagiline	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Antipsychotics</i>		
Aripiprazole	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Antivirals</i>		
HIV protease inhibitors: Amprenavir, Atazanavir, Darunavir, Fosamprenavir, Indinavir, Lopinavir, Nelfinavir, Ritonavir, Saquinavir, Tipranavir	Reduced blood levels with possible loss of HIV suppression.	Do not take with this product.
HIV non-nucleoside reverse transcriptase	Reduced blood levels with possible loss of HIV	Do not take with this product.

inhibitors: Efavirenz, Nevirapine, Delavirdine	suppression	
<i>Anxiolytics</i>		
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.
<i>Barbiturates</i>		
Butobarbital, Phenobarbital	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Calcium Channel Blockers</i>		
Amlodipine, Nifedipine, Verapamil, Felodipine	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Cardiac Glycosides</i>		
Digoxin	Reduced blood levels and loss of control of heart rhythm or heart failure.	Do not take with this product
<i>CNS Stimulants</i>		
Methylphenidate	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Cytotoxics</i>		
Irinotecan, Dasatinib, Erlotinib, Imatinib, Sorafenib, Sunitinib, Etoposide, Mitotane	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Hormonal Contraceptives</i>		
Oral Contraceptives Emergency Hormonal Contraception Hormonal implants and injections Transdermal patches, creams etc. Intra-uterine devices with hormones	Reduced blood levels with risk of unintended pregnancy and breakthrough bleeding.	Do not take with this product.
<i>Hormone Replacement Therapy</i>		
Oral, Transdermal patches, gels, Vaginal rings	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.

<i>Hormone Antagonists</i>		
Exemestane	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Diuretics</i>		
Eplerenone	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>5HT Agonists</i>		
Almotriptan, Eletriptan, Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan and Zolmitriptan	Increased serotonergic effects with increased incidence of adverse reactions.	Do not take with this product.
<i>Immunosuppressants</i>		
Cyclosporin, Tacrolimus	Reduced blood levels with risk of transplant rejection.	Do not take with this product.
<i>Lipid Regulating Medicines</i>		
Simvastatin, Atorvastatin	Reduced blood levels with risk of therapeutic failure.	Do not take with this product
<i>Lithium</i>		
	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Proton Pump Inhibitors</i>		
Lansoprazole, Omeprazole	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Theophylline</i>		
	Reduced blood levels and loss of control of asthma or chronic airflow limitation.	Do not take with this product.
<i>Thyroid Hormones</i>		
Thyroxine	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
<i>Oral Hypoglycaemic drugs</i>		
Gliclazide	Reduced blood levels	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 during pregnancy and lactation is not recommended.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Undesirable effects associated with the use of St. John's wort are generally mild. The following undesirable effects have been reported in clinical studies:

Rare ($>1/10,000 <1/1,000$)

Gastrointestinal disorders:

- Nausea
- Abdominal Pain
- Diarrhoea

Skin and subcutaneous tissue disorders:

- Pruritis
- Rash
- Urticaria

Other ADRs reported in the literature include headaches, neuropathy, anxiety, dizziness, fatigue, mania and allergic reactions.

When St John's wort is used, sunburn-like reactions in the parts of skin exposed to strong UV irradiation (sun, solarium) can rarely occur, particularly in fair-skinned individuals, due to the increased sensitivity of the skin to sunlight (photosensitization).

4.9 Overdose

No cases of overdose have been reported.

When a large overdose has occurred, phototoxic reactions may occur. The skin of the patient should be protected for one week from UV irradiation. 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 established definitely. However, hypericin, pseudohypericin, hyperforin and the flavonoids are considered to play a role in its activity.

5.2 Pharmacokinetic properties

No definitive pharmacokinetic data are available

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

Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Maize starch
Soya polysaccharide
Hydrogenated cotton seed oil

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Amber glass bottle (type III glass), aluminium sealing foil with ionomeric coating and aluminium pilfer proof closure fitted with a polyethylene liner.

Pack sizes: 60 tablets
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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