Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nature's Bounty Hypericum Hard 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.) (5-7:1), corresponding to: 0.3 – 0.9 mg of total hypericins; not less than 18 mg of flavonoids, expressed as rutin; maximum 1 mg hyperforin.
Extraction solvent: ethanol 60% v/v.
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Capsule, hard

Clear, hard, two piece capsules with green brown fill.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

A traditional herbal medicinal product used to relieve the symptoms of slightly low mood in adults, exclusively based upon long-standing use.

4.2 Posology and method of administration

For oral short term use only.

Adults andolder people:
Take 1 capsule daily. Swallow the whole capsule with water.

Duration of use:
If symptoms worsen or persist after 4 weeks of using the medicinal product, a qualified healthcare professional e.g. a doctor or pharmacist should be consulted.

St John's wort should not be used in the treatment of children and adolescents under the age of 18 years (see section 4.4).

4.3 Contraindications

- Hypersensitivity to St. John's wort or any of the excipients listed in section 6.1
- 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, CYP2C9, CYP2C19 and CYP3A4 as well as the transport protein, P-gycoprotein. This results in pharmacokinetic interactions with a large number of medicines including a possible decrease in the effectiveness of those medicines

- Clinically significant pharmacodynamic interactions have been identified with the SSRI antidepressants and the triptan group of medicines used to treat migraine. Due to the increased risk of undesirable serotonergic effects associated with these interactions, this product should not be used concomitantly with these types of medicines (see section 4.5)

- Patients who have undergone transplant surgery and are taking immunosuppressant medicines should not take St. John's wort
- Pregnancy and lactation (See Section 4.6)

- This product should not be used in patients with known dermal photosensitivity or those undergoing phototherapy or any photodiagnostic procedures or during intense ultraviolet (UV) exposure
- Use in the 10 days prior to surgery (see section 4.5 for further details)

4.4 Special warnings and precautions for use

Do not exceed the stated dose.

If symptoms worsen or persist after 4 weeks of using the medicinal product, a qualified healthcare professional e.g. a doctor or pharmacist should be consulted.

This product is intended for the relief of symptoms of slightly low mood. Patients with symptoms and signs of depression should consult a doctor for appropriate treatment. Symptoms of depression include low mood, feelings of helplessness and hopelessness, loss of interest in daily activities, changes in appetite or weight, changes in sleeping patterns, loss of energy, difficulty in concentrating and thoughts of self-harm or suicide.

Suicidal thoughts/suicide

Depression is associated with an increased risk of suicidal thoughts, self-harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

Patients should consult their doctor **before** using St. John's wort if they have previously been diagnosed with a psychiatric illness or are on any medicines for psychiatric illness. St. John's wort should be used with caution in patients with a history of bipolar disorder, mania or hypomania. Patients should consult their doctor if they feel agitated, restless or have thoughts of self-harm or suicide.

Not all St. John's wort products are prepared in the same way. This may affect the composition (e.g. hyperforin and hypericin contents) and consequently the efficacy and safety profile of different St. John's wort products. This should be taken into account when changing between different St. John's wort products.

St. John's wort should be discontinued 10 days prior to elective surgery due to the potential for St. John's wort to interact with drugs used during general and regional anaesthesia. Based on data available for CYP3A, the raised enzyme activity can be expected to return to normal within one week of stopping St. John's wort.

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.

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

4.5 Interaction with other medicinal products and other forms of interactions

Evidence shows that St. John's wort interacts with many medicines; either by affecting drug metabolism or by affecting levels of neurotransmitters.

Substances in St. John's wort 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. When patients stop taking St. John's wort preparations, blood levels of interacting medicines may rise, leading to toxicity.

The concomitant use of St John's wort with certain medicines is contraindicated. These are outlined in the table below.

In addition to the contraindicated medications listed in the table below, special care should be taken in case of concomitant use of certain other medicines. This includes all drug substances whose metabolism is influenced by CYP1A2, CYP2C9, CYP2C19, CYP3A4 or P-glycoprotein because a reduction of plasma concentration is possible. Examples of such drug substances include, but are not limited to, finasteride and fexofenadine.

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 serious adverse reactions from the serotonergic effects associated with these interactions, St. John's wort should not be used concomitantly with these types of medicines.

St John's wort interacts with hormonal contraceptives. This interaction reduces the effectiveness of these contraceptives and increases the risk of unplanned pregnancy. Intracyclic menstrual bleeding may also occur. This applies to all hormonal contraceptives i.e. the oral contraceptive pill, emergency contraceptive pill, hormonal implants, injections or patches. Women using hormonal contraceptives for pregnancy prevention should use additional contraceptive measures. There are currently no data on interactions with hormone-releasing intrauterine devices but this warning should also be taken into consideration when using hormone-releasing intrauterine devices (see sections 4.4 and 4.6).

Table of contraindicated drugs

Co-administered drug	**Interaction**	**Recommendations concerning co-administration**
Anaesthetics/pre-operative medicines		
Fentanyl, propofol, sevoflurane, benzodiazepines E.g. midazolam	Reduced blood levels with risk of therapeutic failure	Based on the elimination half –life of hypericin and hyperforin, this product should be discontinued at least 10 days prior to elective surgery
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, dabigatran, acenocoumarol	Reduced anticoagulant effect and need for increased dose	Do not take with this product
Antidepressants		
Tricyclics E.g. amitriptyline, clomipramine **MAOIs** E.g. moclobemide **SSRIs** E.g. citalopram, escitalopram, fluoxetine, fluvoxamine paroxetine, sertraline **Others** E.g. duloxetine, venlafaxine, bupropion	Increased serotonergic effects with increased incidence of adverse reactions	Do not take with this product

Co-administered drug	Interaction	Recommendations concerning co-administration
Antiepileptics		
All drugs in this class including: carbamazepine, phenobarbital phenytoin, primidone, sodium valproate	Reduced blood levels with risk of increased 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-Parkinson's		
Rasagiline	Reduced blood levels with risk of therapeutic failure	Do not take with this product
Antiplatelets		
Clopidogrel	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: Amprenavir, atazanavir, darunavir, fosamprenavir indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, tipranavir	Reduced blood levels with risk of therapeutic failure	Do not take with this product
HIV non-nucleoside reverse transcriptase inhibitors: Efavirenz, nevirapine, delavirdine	Reduced blood levels with risk of therapeutic failure	Do not take with this product
Anxiolytics		
Buspirone	Increased serotonergic effects with increased incidence of adverse events	Do not take with this product
Benzodiazepines E.g. midazolam	Reduced blood levels with risk of therapeutic failure	Do not take with this product
Aprepitant	Reduced blood levels with risk of therapeutic failure	Do not take with this product
Barbiturates		
Phenobarbital	Reduced blood levels with risk of therapeutic failure	Do not take with this product

Co-administered	Interaction	Recommendations

drug		concerning co-administration
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		
Methyl phenidate	Reduced blood levels with risk of therapeutic failure	Do not take with this product
Cytotoxics		
Irinotecan, dasatinib, erlotinib, imatinib, sorafenib, sunitinib, etoposide, mitotane, docetaxel	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
Hormonal contraceptives		
Oral contraceptives Emergency hormonal contraception Hormonal implants and injections Transdermal patches Intra-uterine devices with hormones	Reduced blood levels with risk of unintended pregnancy and breakthrough bleeding.	Do not take with this product
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

Co-administered drug	Interaction	Recommendations concerning co-administration
5HT agonists		
Almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, and zolmitriptan	Increased serotonergic effects with increased incidence of adverse reactions	Do not take with this product
Immunosuppressants		
Cyclosporin, tacrolimus for systemic use	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
Oral hypoglycaemic drugs		
Gliclazide	Reduced blood levels with risk of therapeutic failure.	Do not take with this product
Opiates		
Tramadol, methadone, oxycodone	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 with risk of therapeutic failure	Do not take with this product
Thyroid hormones		
Thyroxine	Reduced blood levels with risk of therapeutic failure	Do not take with this product

4.6 Fertility, pregnancy and lactation

The safety of St John's wort during pregnancy and lactation has not been established. Animal studies have shown equivocal results with regard to reproductive toxicity, with some data suggesting that hypericin (one of the constituents of St John's wort) may have teratogenic effects. In the absence of sufficient data, use of St John's Wort during pregnancy and lactation should be avoided.

Fertility

No data available

Women of child-bearing potential

St John's wort interacts with hormonal contraceptives. This interaction reduces the effectiveness of these contraceptives and increases the risk of unplanned pregnancy. Intracyclic menstrual bleeding may also occur. This applies to all hormonal contraceptives i.e. the oral contraceptive pill, emergency contraceptive pill, hormonal implants, injections or patches. Women using hormonal contraceptives for pregnancy prevention should use additional contraceptive measures. There are currently no data on interactions with hormone-releasing intrauterine devices but this warning should also be taken into consideration when using hormone-releasing intrauterine devices (see section 4.4 and 4.5).

4.7 Effects on ability to drive and use machines

Adequate studies of the effects on the ability to drive and use machines have not been performed. In rare cases St John's wort may cause dizziness or drowsiness. If affected, patients should not drive or operate machinery.

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 qualified healthcare professional e.g. a doctor or pharmacist 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms and signs
After the intake of 4.5 g St John's wort dry extract per day for 2 weeks and an additional 15 g St John's wort dry extract just before hospitalisation, seizures and confusion have been reported in one case.

Management of overdose
When a large overdose of St John's wort has occurred, phototoxic skin reactions may occur. The skin of the patient should be protected from UV irradiation and sunlight for 1-2 weeks. 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, as amended.

5.2 Pharmacokinetic properties

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

5.3 Preclinical safety data

Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC, as amended. The following data has been presented in support of this product.

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 with some data suggesting that hypericin (one of the constituents of St. John's wort) may have tetraogenic effects.

Tests on the carcinogenic potential have not been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Magnesium stearate
Silica colloidal hydrated

Inactive ingredients (excipients) in the dry extract:
Maltodextrin
Silica colloidal anhydrous

Capsule Shell:
Hypromellose

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store the capsules above 25ºC.
Keep the bottle tightly closed in order to protect from light and moisture.

6.5 Nature and contents of container

Green polyethylene terephthalate (PET) bottles with a polypropylene cap and an inner seal liner made up of polyester, polymer adhesive layer, polyolefin foam and aluminium foil.

Pack size: 50 hard capsules and 100 hard capsules
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 REGISTRATION HOLDER

Holland & Barrett Limited
Cedar Drive
Dublin Airport Logistics Park
Saint Margarets
Co Dublin
K67 E0C5
Ireland

8 REGISTRATION NUMBER(S)

TR23157/004/001

9 DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

Date of first registration: 11th of November 2016.

10 DATE OF REVISION OF THE TEXT

February 2021