BIO-HEALTH

Hyperidrine®

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

Bio-Health Ltd. Culpeper Close, Medway City Estate, Rochester, Kent ME2 4HU
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SECTION 1 - NAME OF THE MEDICINAL PRODUCT

HYPERIDRINE Capsules

SECTION 2 - QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 300mg of St John's Wort aerial parts (*Hypericum perforatum* L.)
For full list of excipients see section 6.1.

SECTION 3 - PHARMACEUTICAL FORM

Hard capsules.
Clear size 0 hard capsules.

SECTION 4 - CLINICAL PARTICULARS

SECTION 4.1 - Therapeutic Indications

Hyperidrine is a traditional herbal medicinal product used to relieve the symptoms of slightly low mood and mild anxiety, based on traditional use only.

SECTION 4.2 - Posology and method of administration

For oral short term use only. Adults and the Elderly: Take one capsule three times a day, swallowed with water. The patient should consult a doctor or qualified healthcare practitioner if symptoms worsen or do not improve after 6 weeks. Not recommended for children or adolescents under 18 years (See Section 4.4 Special warnings and precautions for use).

SECTION 4.3 - Contra-indications

Hypersensitivity to St John's Wort or any of the excipients.

Hyperidrine should not be used in patients with known dermal photosensitivity or those undergoing phototherapy or any photodiagnostic procedures.

Hyperidrine should not be taken concomitantly with any of the medicines specified in section 4.5. This is because St. John's wort (*Hypericum performatum*) has been shown to induce the cytochrome P450 isoenzymes CYP1A2, CYP2C19, CYP2C9 and CYP3A4 as well as the transport protein P-glycoprotein. This results in pharmacokinetic interactions with a large number of medicines including a possible decrease in the effectiveness of those medicines.

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

SECTION 4.4 - Special Warnings and Precautions for Use

Do not exceed the stated dose.

The use of Hyperidrine is not recommended for children and adolescents under 18 years of age because data are not sufficient and medical advice should be sought.

If the condition worsens or if symptoms persist for more than 6 weeks medical advice should be sought.

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

In very rare cases, particularly in fair-skinned individuals, sunburn type reactions may occur on skin areas exposed to strong sunlight due to photosensitisation by St. John's Wort. Patients taking Hyperidrine should avoid excessive sunbathing or the use of sunbeds or solariums.

Hyperidrine should be discontinued at least 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.

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SECTION 4.5 - Interaction with other medicaments and other forms of interaction

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

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

Special care should be taken in case of concomitant use of all drug substances the metabolism of which is influenced by CYP1A2, CYP3A4, CYP2C9, CYP2C19 or P - glycoprotein (e.g. amitriptyline, fexofenadine, benzodiazepines, methadone, simvastatin, digoxin, finasteride), because a reduction of plasma 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, Hyperidrine (St John's Wort) should not be taken concomitantly with the Medicines included in the following table.

CO-ADMINISTERED DRUG	INTERACTION	RECOMMENDATIONS CONCERNING ADMINISTRATION
Anaesthetic/pre-operative medicines		
Fentanyl, propofol, sevoflurane, midazolam	Reduced blood levels with risk of therapeutic failure.	Based on the elimination half-lives of Hypericum and hyperforin this product should be discontinued at least 10 days prior to 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, acenocoumarol	Reduced anticoagulant effect and need for increased dose.	Do not take with this product.

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Antidepressants		
Tricyclics eg: amitriptyline, clomipramine **MAOIs** eg Moclobemide **SSRIs** 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: 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 inhibitors: efavirenz nevirapine delavirdine	Reduced blood levels with possible loss of HIV suppression.	Do not take with this product.

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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		
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	Reduced blood levels with risk of therapeutic failure.	Do not take with this product.
Hormonal contraceptives		
Oral contraceptives Emergency hormonal contraception Hormonal implants, injections Transdermal patches, creams etc Intra-uterine devices with hormones	Reduced blood levels with a risk of unintended pregnancy and breakthrough bleeding.	Do not take with this product.

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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		
Alomotriptan eletriptan frovatriptan naratriptan rizatriptan sumatriptan and zolmitriptan	Increased serotonergic effects with increased incidence of adverse reactions.	Do not take with this product.
Immunosuppressants		
Ciclosporin tacrolimus	Reduced blood levels with a risk of transplant reaction.	Do not take with this product.
Lipid regulating drugs		
Simvastatin atorvastatin	Reduced blood levels with a risk of therapeutic reaction.	Do not take with this product.
Lithium	Reduced blood levels with a risk of therapeutic reaction.	Do not take with this product.
Proton pump inhibitors		
Lansoprazole omeprazole	Reduced blood levels with a risk of therapeutic reaction.	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 a risk of therapeutic reaction.	Do not take with this product.
Oral hypoglycaemic drugs		
Gliclazide	Reduced blood levels with a risk of therapeutic reaction.	Do not take with this product.

- **SECTION 4.6 - Pregnancy and Lactation**

The safety of Hyperidrine (St John's Wort) during pregnancy and lactation has not been established. In the absence of sufficient data, use during pregnancy and lactation is not recommended.

- **SECTION 4.7 - Effects on ability to drive and use machines**

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

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SECTION 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.

SECTION 4.9 - Overdose

No cases of overdose have 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.

SECTION 5 - PHARMACOLOGICAL PROPERTIES

SECTION 5.1 - Pharmacodynamic Properties

Pharmacotherapeutic group: Herbal medicinal product for treatment of depressive disorders.

ATC Code: N06AX

The active constituents of Hyperidrine (St John's Wort) have not been definitively established. However, hypericin, pseudohypericin hyperforin and the flavonoids are considered to have synergistic activity.

SECTION 5.2 - Pharmacokinetic Properties

No definitive pharmacokinetic data available.

The active ingredients of Hyperidrine (St John's Wort) can interact with other medicinal agents in two ways. Firstly, active ingredients in Hyperidrine (St John's Wort) themselves are metabolised in the liver by the CYP3A isoenzymes, 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 Hyperidrine (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.

SECTION 5.3 - Preclinical safety data

Tests on reproductive toxicity and carcinogenicity have not been preformed. Adequate information is currently not available on genotoxicity.

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 pigmentation was significantly reduced. In the recommended dosage, no signs of photoxicity are reported.

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SECTION 6 - PHARMACEUTICAL PARTICULARS

SECTION 6.1 - List of excipients

Hypromellose (Capsule shell).

SECTION 6.2 - Incompatibilities

Not Applicable.

SECTION 6.3 - Shelf-life

The shelf life of Hyperidrine is 3 years.

SECTION 6.4 - Special Precautions for storage

Store below 25°C in the original packaging.

SECTION 6.5 - Nature and contents of container

Duma 110ml HDPE plastic bottle and tamper evident threaded Duma cap.
Duma 200ml HDPE plastic bottle and tamper evident press on Duma cap.

Hyperidrine pack contains 60 or 120 Capsules.

SECTION 6.6 - Special precautions for disposal

There are no special precautions for disposal of Hyperidrine capsules. When the container is empty the label should be removed and the bottle placed in a recycling bin.

SECTION 7 - MARKETING AUTHORISATION HOLDER

Bio-Health Limited
Culpeper Close
Medway City Estate
Rochester
Kent
ME2 4HU

SECTION 8 - MARKETING AUTHORISATION NUMBER(S)

THR 15817/0006

SECTION 9 - DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29/09/2010

SECTION 10 - DATE OF REVISION OF THE TEXT

29/09/2010

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