

# **SUMMARY OF PRODUCT CHARACTERISTICS**

## **BOTANOVA TABLETS**

### **1 NAME OF THE MEDICINAL PRODUCT**

BOTANOVA, Film-coated tablets

### **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each film-coated tablet contains:

60 mg of extract (as dry extract) from St John's Wort Herb (*Hypericum perforatum* L.) (4.6-6.5:1),

Extraction solvent: ethanol 38% (m/m);

28 mg of extract (as dry extract) from Valerian Root (*Valeriana officinalis* L.) (3.8-5.6:1),

Extraction solvent: ethanol 40% (m/m);

32 mg of extract (as dry extract) from Passion Flower Herb (*Passiflora incarnata* L.) (6.25-7.1:1),

Extraction solvent: ethanol 60% (m/m)

Each film-coated tablet also contains:

Lactose monohydrate (90.5 mg) and glucose (10.4 mg).

For a full list of excipients, see section 6.1.

### **3 PHARMACEUTICAL FORM**

Film-coated tablets.

Light blue, biconvex, round, film coated tablets.

### **4 CLINICAL PARTICULARS**

#### **4.1 Therapeutic indications**

Traditional herbal medicinal product used to relieve:

- slightly low mood and mild anxiety,
- sleep disturbances due to symptoms of mild anxiety,

based on traditional use only.

#### **4.2 Posology and method of administration**

*Adults and the elderly*

*To help relieve symptoms of slightly low mood and mild anxiety:*

Two tablets to be taken orally one to three times daily.

*To relieve sleep disturbances due to symptoms of mild anxiety:*

Two tablets to be taken orally before going to sleep.

The tablets should be swallowed whole with some liquid.

Not for children or adolescents less than 18 years old.

**Duration of use**

Not for long term-use. The patient should consult a doctor if symptoms worsen or do not improve after 6 weeks.

**4.3 Contraindications**

Hypersensitivity to any of the active ingredients or any of the excipients.

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

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 some of these 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 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 is intended for relief of slightly low mood and mild anxiety and of sleep disturbances due to symptoms of mild anxiety. Patients with signs and symptoms of depression should seek medical advice for appropriate treatment.

In very rare cases, particularly in light-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 medicines used during general and regional anaesthesia (see Section 4.5)

Patients with rare glucose-galactose malabsorption and/or with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucosegalactose malabsorption should not take this medicine.

#### 4.5 Interaction with other medicinal products and other forms of interaction

Substances in St John's Wort have been shown to induce the cytochrome P450 (CYP) isoenzymes CYP1A2, CYP2C9, and CYP3A4 and the drug transport protein P-glycoprotein. This results in pharmacokinetic interactions with a large number of medicines leading to a potential decrease in the effectiveness of some of these medicines. Clinically significant interactions have been reported with, for example: warfarin, cyclosporin, 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.

In accordance with the above considerations, BOTANOVA should not be taken concomitantly with the medicines included in the 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	Do not take with this product.

	with risk of therapeutic failure.	
<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>		
<b>Tricyclics</b> e.g. Amitriptyline, Clomipramine <b>MAOIs</b> e.g. Moclobemide <b>SSRIs</b> e.g. Citalopram, Escitalopram, Fluoxetine, Fluvoxamine, Paroxetine, Sertraline <b>Others</b> e.g. Duloxetine, Venlafaxine	Increased serotonergic effects with increased incidence of adverse reactions.	Do not take with this product.
<i>Antiepileptics</i>		
<b>All drugs in this class including:</b> 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.

	failure.	
<i>Antivirals</i>		
<b>HIV protease inhibitors:</b> 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.
<b>HIV non-nucleoside reverse transcriptase inhibitors:</b> Efavirenz, Nevirapine, Delavirdine	Reduced blood levels with possible loss of HIV suppression	Do not take with this product.
<i>Anxiolytics</i>		
Bupirone	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	Reduced blood levels with risk of unintended	Do not take with this product.

Contraception Hormonal implants and injections Transdermal patches, creams etc. Intra-uterine devices with hormones Vaginal rings	pregnancy and breakthrough bleeding.	
<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 during pregnancy and lactation has not been established. In the absence of sufficient data, taking BOTANOVA during pregnancy and lactation is not recommended.

#### 4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. In rare cases BOTANOVA may cause tiredness; if affected do not drive or operate machinery.

#### 4.8 Undesirable effects

High-doses of St John's Wort extracts may, especially in fair-skinned individuals, lead to increased sensitivity to sunlight (photosensitization) and, therefore, produce sunburn-like reactions of skin areas exposed to intense sunlight.

There have been rare reports, following intake of St John's Wort, of gastrointestinal symptoms, allergic reactions, fatigue or restlessness. Gastrointestinal adverse drug reactions that have been reported include dyspepsia, anorexia, nausea, diarrhoea and constipation. Other ADRs reported in the literature include headaches, neuropathy, anxiety, dizziness, mania and allergic reactions.

If other adverse reactions occur, a doctor or qualified healthcare practitioner should be consulted.

#### 4.9 Overdose

No cases have been documented for overdose of BOTANOVA.

There are no data on human overdose with St John's Wort. Where 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

Pharmacotherapeutic group: **antidepressive and anxiolytic traditional herbal medicinal product**

**ATC code:** NO6AP51

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.

No studies of the pharmacokinetics of the total extract have been carried out.

Studies of the pharmacokinetics of specific constituents of St John's Wort (hypericin, pseudohypericin) considered marker substances indicate that onset of absorption is approximately 0.3 to 2.6 hours after oral dosing, and that the blood plasma concentrations of these constituents of St John's Wort are dose-related.

#### **Valerian Root and Passion Flower Herb**

No specific studies of Valerian Root extract and Passion Flower Herb extract are available.

### **5.3 Preclinical safety data**

There is no evidence that BOTANOVA, or its constituent herbal extracts, exert any toxic effects. The traditional-use of the individual constituent herbs, as well as the clinical use BOTANOVA have not revealed significant evidence of any toxicity. Modern standard tests performed on BOTANOVA revealed no evidence of any genotoxicity. Tests on reproductive toxicity and carcinogenicity have not been performed on extracts of St. John's wort, Passion flower or Valerian.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Excipients of the herbal preparation:

Lactose monohydrate  
glucose, liquid, spray-dried  
maltodextrin  
silica, colloidal anhydrous.

Excipients of the tablet:

Lactose monohydrate  
silica, colloidal anhydrous  
talc;

magnesium stearate

povidone K30

glycerol (85 per cent)

croscarmellose sodium.

Excipients of the film coating:

Basic butylated methacrylate copolymer  
talc

titanium dioxide (E 171)

indigo carmine laquer (E 132)

macrogol 6000

magnesium stearate.

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

2 years.

**6.4 Special precautions for storage**

Do not store above 30°C. Keep the Blister in the outer carton in order to protect from light.

**6.5 Nature and contents of container**

Aluminium/PVC/Aclar-blisters; containing 20 film-coated tablets per blister.  
Original packs of  
20, 60, and 100 film-coated tablets

**6.6 Special precautions for disposal**

No special requirements.

**7 MARKETING AUTHORISATION HOLDER**

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