SUMMARY PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

BUSPON 5 mg capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule;

Active substance:

Buspirone hydrochloride 5.0 mg

Excipient(s):

Lactose 94 mg

Tartrazine (E102)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule,

Body white opaque, cap blue opaque hard gelatin capsules (no:3) with homogeneous powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BUSPON is used for the symptomatic treatment of generalized anxiety.

4.2 Posology and method of administration

Posology/frequency and duration of administration:

Treatment is initiated with 5 mg buspirone 2-3 times daily. The optimum dose varies between 15-30 mg daily (in divided doses). The maximum daily dose should not exceed 45 mg.

The dose should be reduced in renal or hepatic impairment.

Method of administration:

BUSPON capsules are for oral administration.

Additional information on special populations:

Renal/Liver failure:

The dose should be reduced in renal or hepatic disorders.

Pediatric population: Should not be used by people under 18 years of age.

Geriatric population: As in adults.

4.3 Contraindications

It should not be used in patients with impaired hepatic and renal function (creatinine clearance of 20 ml/min or less or plasma creatinine level above 200 µmol/l), in patients in a state of stagnation, in patients with hypersensitivity to buspirone or its components, have acute narrow angle glaucoma, myasthenia gravis, epilepsy and pregnancy.

4.4 Special warnings and precautions for use

Anxiety and tension due to the stresses of daily life do not require the use of any anxiolytic.

Since there is limited experience with the use of buspirone to date and there is no literature on the safety and efficacy of long-term use, high dose toxicity, use in

children and the elderly, the points mentioned in the side effects section should be carefully considered until the information that may guide the use of the substance is finalized.

Monitoring of the patient: Plasma levels do not need to be determined. Buspirone shows non-linear pharmacokinetic properties. Increasing the dosage may increase the plasma concentration disproportionately to the dose given. Therefore, the dosage should be increased by no more than 5 mg every 2 or 3 days. The patient should be carefully monitored for side effects (e.g. sedation, dysphoria, dizziness, gastrointestinal complaints, etc.).

Concomitant use with MAO inhibitors is not recommended as they may cause hypertensive reactions.

Buspirone causes a low rate of sedation compared to other anxiolytics.

Since there is no cross-tolerance between buspirone and benzodiazepines and sedative/hypnotic drugs, Buspirone does not prevent withdrawal reactions that may occur with abrupt discontinuation of these drugs. Therefore, such drugs should not be discontinued abruptly, treatment should be discontinued by gradually decreasing the dose and then buspirone should be started.

Since buspirone is metabolized in the liver and excreted from the kidneys, it is not recommended for use in severe kidney and liver disorders.

People with the following rare inherited diseases should not take buspirone:

- Galactose intolerance, Lapp lactose insufficiency or glucose - galactose malabsorption

May cause allergic reactions as it contains tartrazine in its formula.

Alcohol use should be avoided.

4.5 Interactions with other medicinal products and other forms of interaction

It should not be used in combination with MAO inhibitors (phenelzine and tranylcypramine) as an increase in blood pressure may occur.

In vitro studies have shown that buspirone does not alter the localization of warfarin, phenytoin or propranolol in plasma proteins.

No interaction with amitriptyline has been observed. A slight increase in the metabolites of diazepam was observed. Buspirone is metabolized (in vitro) by the cytochrome CYP3A4 enzyme system. Interactions between buspirone and erythromycin, itraconazole, nefazodone, grapefruit juice, diltiazem and verapamil, which are inhibited by this isoenzyme, have also been observed. The dose of buspirone should be reduced when used with such potent CYP3A4 inhibitors. Decreased plasma concentrations and pharmacodynamic effects of buspirone have been observed when used with rifampicin, a CYP3A4 inducer.

Baclofen, lofexidine, nabilone, antihistamines may increase the sedative effect.

An increase in SGPT was observed when used with trazodone. When used with haloperidol, serum haloperidol concentrations increase.

Buspirone can bind to the sites of drugs that bind weakly to blood proteins such as digoxin and release them.

Although there is no evidence of interaction with alcohol, concomitant use should be avoided.

Since it increases plasma prolactin levels at high doses, this situation should be taken into consideration in diagnostic tests.

Caution should be exercised in combination with serotonergic drugs: (MAOIs, L-tryptophan, triptans, tramadol, linezolid, SSRIs, lithium and St. John's Wort. If serotonin syndrome is suspected during treatment with SSRIs, buspirone should be discontinued immediately and supportive symptomatic treatment initiated.)

4.6 Pregnancy and lactation

General recommendation

Pregnancy Category: B

Women of childbearing potential / Birth Control (Contraception):

No data on exposure during pregnancy are available for buspirone hydrochloride.

Animal studies do not indicate direct or indirect harmful effects in relation to pregnancy / embryonal / fetal development / parturition or postnatal development. (See Section 5.3)

Caution should be exercised when given to pregnant women.

Pregnancy:

Since there are no adequate and controlled studies in pregnant women, use in pregnancy (especially in the first trimester) should be avoided unless deemed mandatory by the doctor.

Lactation:

The extent of excretion into breast milk is not known. However, it has been observed that buspirone and its metabolite pass into milk in rats. Therefore, this feature should be taken into consideration in breastfeeding. It should not be given during breastfeeding unless deemed necessary.

Reproductive ability/Fertility

Animal studies have not shown any effect on reproductive ability.

4.7 Effects on ability to drive and use machines

Since transient adverse effects may be seen in the early period, the patient should avoid driving and using machines that require attention until the adverse effects of the drug are no longer affected.

4.8 Undesirable effects

Buspirone is generally well tolerated. Side effects usually occur at the beginning of treatment and can be reduced with continued use and/or dose reduction.

The most common side effects in buspirone treatment compared to placebo:

Central Nervous System: Drowsiness, dizziness, EPS, serotonin syndrome, headache, excitement, nervousness, feeling of lightness.

Dermatologic: Rash.

Gastrointestinal System: Diarrhea, nausea.

Neuromuscular System: Muscle weakness, numbness, lack of coordination.

Special Senses: Blurred vision.

In addition, tachycardia, palpitation, chest pain, a feeling of complacency, confusion, seizures, dry mouth, fatigue and sweating are rarely reported side effects.

Tinnitus, nasal congestion and sore throat are side effects of unknown frequency.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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 in accordance with local requirements.

4.9 Overdose

Characteristics:

Symptoms include nausea, vomiting, headache, dizziness, drowsiness, tinnitus and restlessness. Mild bradycardia and hypotension have been reported. Extrapyramidal symptoms have been reported after use at therapeutic doses. Rarely convulsions may occur.

Management:

Treatment should be symptomatic and supportive. The benefits of gastric decontamination are uncertain. If the patient has been exposed to more than 5 mg/kg of buspirone and no drowsiness has occurred within a maximum of 1 hour, treatment with activated charcoal may be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anxiolytics

ATC code: N05BE01

Buspirone is an azaspirodecandione derivative. Although the mechanism of action of buspirone is not completely clear, it is an anxiolytic with a completely different mechanism of action and chemical structure than benzodiazepines. Buspirone is a partial agonist of 5-HT_{1A} receptors and its anxiolytic effect is thought to occur in this way. Buspirone has been shown to have no affinity for benzodiazepine receptors and does not affect GABA binding. It does not have the anticonvulsive, sedation and muscle relaxant effects of benzodiazepines.

Buspirone decreases serotonin and acetylcholine activity but increases the activity of specific noradrenergic and dopaminergic pathways. It blocks the stereotypy produced by apomorphine. Although it increases prolactin levels in high doses, it lacks this effect in therapeutic doses.

5.2 Pharmacokinetic properties

Absorption

It is rapidly absorbed after oral doses but largely undergoes first-pass metabolism.

Distribution

Peak plasma levels are reached 60-90 minutes after ingestion. Plasma concentrations are linearly related to dose. Steady-state plasma concentrations are reached within 2 days following multiple doses. Buspirone is 95% bound to proteins.

Biotransformation

Buspirone is metabolized in the liver by the enzyme CYP3A4. Its metabolites are 5-hydroxy buspirone and 1-primidinyl piperazine. The latter is the active metabolite and has 1-20% of the activity of the parent compound. The mean plasma half-life ranges from 2-11 hours.

Excretion

0.1% is excreted unchanged in the urine. Of the amount absorbed, 60-67% is excreted in the urine and the remainder in the feces.

5.3 Preclinical safety data

In reproduction studies in rats and mice, administration of buspirone at a dose 30 times higher than the maximum recommended dose for humans did not cause any damage to the fetus and did not cause fertility impairment.

In a 24-month study in rats 133 times higher than the maximum recommended dose for humans or in an 18-month study in mice 167 times higher than the maximum recommended dose for humans, no evidence of carcinogenic potential was found.

Studies have shown that buspirone is not mutagenic.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch

Magnesium stearate

Titanium dioxide (E171)

Erythrocin (E127)

Indigotine (E132)

Gelatin

6.2 Incompatibilities

None.

6.3 Shelf life

60 months

6.4 Special precautions for storage

Store at room temperature below 25 oC.

6.5 Nature and contents of the container

Blisters of 25 capsules with transparent PVC on one side and printed on the other side.

Each carton box contains 25 or 50 capsules.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER

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8. MARKETING AUTHORIZATION NUMBER

143/71

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

Date of First authorization: 05.01.1988

Date of last renewal: 10.03.2004

10. DATE OF RENEWAL OF THE SPC