

## BUSPIRONE VIATRIS

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### 1. Product Name

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BUSPIRONE VIATRIS, 5 mg and 10 mg, tablet.

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### 2. Qualitative and Quantitative Composition

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Each tablet contains 5 mg or 10 mg of buspirone hydrochloride.

**Excipient with known effect:**

Sugars as lactose.

For the full list of excipients, see section 6.1.

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### 3. Pharmaceutical Form

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5 mg tablets: white, round bevel edged tablet, 7 mm in diameter embossed "BR 5" embossed on one side and "G" on the other side.

10 mg tablets: white, 11 mm x 5.5 mm capsule shaped tablet embossed "BR/10" on one side and "G" on the other side.

Please note: "BR/10" is a written representation of the embossing "BR" score line "10"

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### 4. Clinical Particulars

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#### 4.1 *Therapeutic indications*

Buspirone hydrochloride is indicated for the management of anxiety disorders or the short-term relief of symptoms of anxiety with or without accompanying depression. The diagnosis of patients studied in controlled clinical trials of buspirone corresponds to the Generalised Anxiety Disorder of the WHO classification as described below:

Generalised, persistent anxiety is manifested by symptoms from three of the following four categories:

**General tensions:** shakiness, jitteriness, jumpiness, trembling, tension, muscle aches, fatigability, inability to relax, eyelid twitch, furrowed brow, strained face, fidgeting, restlessness, easy startle.

**Autonomic hyperactivity:** sweating, heart pounding or racing, cold clammy hands, dry mouth, dizziness, lightheadedness, paraesthesias (tingling in hands or feet), upset stomach, hot or cold spells, frequent urination, diarrhoea, discomfort in the pit of the stomach, lump in the throat, flushing, pallor, high resting pulse and respiration rate.

**Apprehensive expectations:** anxiety, worry, fear, rumination, and anticipation of misfortune to self or others.

**Vigilance and scanning:** hypertensiveness resulting in distractibility, difficulty in concentrating, insomnia, feeling "on edge", irritability, impatience.

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The anxious mood has been continuous for at least one month. The ordinary anxiety and tension associated with the stress of everyday life usually does not require treatment with an anxiolytic agent.

Controlled clinical studies of buspirone have been limited to six months.

## **4.2 Dose and method of administration**

The usual starting dose is 5 mg given three times daily. This may be titrated according to the needs of the patient and the daily dose increased by 5 mg increments every two or three days depending upon the therapeutic response to a maximum daily dose of 60 mg. After dosage titration the usual daily dose will be 20 to 30 mg per day in divided doses.

Food increases the bioavailability of buspirone. Buspirone should be taken at the same time each day and consistently with or without food (see section 5.2).

If buspirone is given with a potent inhibitor of CYP3A4 such as itraconazole or nefazodone, the initial dose of buspirone should be reduced and titrated based on clinical assessment (see section 4.5).

Grapefruit juice increases the plasma concentrations of buspirone. Patients taking buspirone should avoid consuming grapefruit juice (see section 4.5).

## **Special populations**

### ***Renal or hepatic impairment***

The dose should be reduced in renal or hepatic impairment but buspirone should not be used in patients with severe renal or hepatic impairment (see section 4.4).

## **4.3 Contraindications**

BUSPIRONE VIATRIS should not be administered in case of

- Hypersensitivity to the active substance buspirone hydrochloride or any of the inactive ingredients listed in section 6.1.
- Acute angle-closure glaucoma
- Myasthenia gravis
- Epilepsy
- Acute intoxication with alcohol, hypnotics, analgesics, or antipsychotic medicines
- Severe hepatic insufficiency
- Severe renal insufficiency (eGFR < 20ml/min/1.73m<sup>2</sup>).

## **4.4 Special warnings and precautions for use**

Note

Not all states of anxiety require medical treatment. They may also be a result of physical or mental illness and may sometimes be cured by targeted treatment of the underlying disease.

In clinical and experimental studies, there has been no indication that buspirone causes the risk of developing habituation or addiction. Nevertheless, until further clinical experience is gained, the administration should be monitored accordingly. Buspirone should be used with caution in patients with drug dependence.

Buspirone should be used with caution in patients with hepatic or renal impairment:

### **Renal Impairment**

Buspirone should be used cautiously in patients with renal disease. Since buspirone is excreted by the kidneys the dose should be reduced in patients with renal impairment but administration of buspirone to patients with severe renal impairment cannot be recommended.

## **Hepatic impairment**

Buspirone should be used cautiously, at reduced doses, in patients with impaired hepatic function or may be contraindicated (see section 4.3). Buspirone clearance is reduced in patients with hepatic cirrhosis. In one study, a single 20 mg oral dose led to 16 fold and 13 fold increases in mean peak buspirone blood levels and mean peak AUC respectively in cirrhotic patients compared to normal volunteers. Administration of buspirone to patients with severe hepatic impairment is not recommended.

## **Previous benzodiazepine treatment and potential for withdrawal reactions in sedative/hypnotic/anxiolytic drug-dependent patients**

Because buspirone has no cross-tolerance to benzodiazepines and other sedatives/hypnotics, it will not block the withdrawal symptoms that often occur at the discontinuation of these preparations. Therefore, before starting treatment with buspirone, these medicines should be discontinued gradually. This has particular relevance to patients who have taken a medicinal product with calming effect on the CNS for a long time. Careful observation is recommended for the use of buspirone in patients with a history of seizures.

## **Convulsive disorders**

In individual cases, seizures were reported when taking buspirone and SSRIs concurrently (see section 4.5)

## **Monoamine oxidase inhibitors**

A combination of buspirone with MAOIs is not recommended because of the risk of hypertensive reactions (see section 4.5).

The concomitant use of buspirone with other CNS-active medicines should be approached with caution (see section 4.5).

## **Long-term treatment**

If a long-term medical treatment is necessary, it should be monitored intensively. The need to continue treatment should be periodically reassessed by discontinuation of treatment after a longer period of time (several months).

Psycho- and psychotherapeutic measures should not be neglected during the treatment with buspirone.

Since the mechanism of action of buspirone is not fully known, the long-term toxic effects on the central nervous system or other body systems cannot be predicted. Controlled clinical studies with buspirone have only been performed over a period of six months.

## **Central dopaminergic receptor binding**

The possibility of acute and chronic changes in dopamine mediated neurological function (e.g. dystonia, pseudo-Parkinsonism, akathisia and tardive dyskinesia) should be considered since animal studies have shown that buspirone can bind to central dopamine receptors.

## **Paediatric use**

The safety and effectiveness of buspirone in children and adolescents below the age of 18 years as the safety and efficacy has not been established in this age group (see sections 5.1 and 5.2).

## **Excipients**

BUSPIRONE VIATRIS contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this product.

## **4.5 Interaction with other medicines and other forms of interaction**

There are not sufficient data available regarding the concomitant use with other anxiolytics/sedatives and other centrally acting agents (e.g. antipsychotics and antidepressants), as well as antihypertensives, antidiabetics, anticoagulants, contraceptives and cardiac glycosides. Therefore, the concomitant use of buspirone with these medicinal products should be monitored carefully.

### **Effect of other medicines on buspirone**

#### ***Association not recommended***

##### **Monoamine oxidase inhibitors**

Co-administration of buspirone and monoamine oxidase inhibitors (phenelzine sulfate or tranylcypromine sulfate) may cause increases in blood pressure. Therefore, it is recommended that buspirone not be used concomitantly with a monoamine oxidase inhibitor (MAOI) (see section 4.4).

##### **Erythromycin**

The co-administration of buspirone (10 mg as a single dose) and erythromycin (1.5 g/day for 4 days) to healthy volunteers increased plasma buspirone concentrations (5-fold increase in  $C_{max}$  and a 6-fold increase in AUC), probably due to CYP3A4 inhibition. If buspirone and erythromycin are to be used in combination, a low dose of buspirone (e.g. 2.5 mg twice a day) is recommended. Subsequent dose adjustments of either drug should be based on clinical response.

##### **Itraconazole**

The co-administration of buspirone (10 mg as a single dose) and itraconazole (200 mg once daily for 4 days) to healthy volunteers increased plasma buspirone concentrations (13-fold increase in  $C_{max}$  and a 19-fold increase in AUC) probably due to CYP3A4 inhibition.. If buspirone and itraconazole are to be used in combination, a low dose of buspirone (e.g. 2.5 mg once a day) is recommended. Subsequent dose adjustments of either drug should be based on clinical response.

#### ***Association with precautions of use***

##### **Diltiazem**

In a study of healthy volunteers, administration of buspirone (10 mg as a single dose) with diltiazem (60 mg three times a day) increased plasma buspirone concentrations. The  $C_{max}$  and AUC of buspirone were increased 5.3-fold and 4-fold, respectively, probably due to inhibition of CYP3A4 first-pass metabolism. Enhanced effects and increased toxicity of buspirone may be possible when buspirone is administered with diltiazem. Subsequent dose adjustments of either medicine should be based on clinical response.

##### **Verapamil**

In a study of healthy volunteers, administration of buspirone (10 mg as a single dose) with verapamil (80 mg three times a day) increased plasma buspirone concentrations. The AUC and  $C_{max}$  of buspirone were increased 3.4-fold, probably due to inhibition of CYP3A4 first-pass metabolism. Enhanced effects and increased toxicity of buspirone may be possible when buspirone is administered with verapamil. Subsequent dose adjustments of either medicine should be based on clinical response.

##### **Rifampicin**

Rifampicin induces the metabolism of buspirone via CYP3A4. Therefore in a study in healthy volunteers, co-administration of buspirone (30 mg as a single dose) with rifampicin (600 mg once daily for 5 days) decreased the plasma concentrations (84% decrease in  $C_{max}$  and 90% decrease in AUC) and pharmacodynamic effects of buspirone

## **Associations to be taken into account**

### **Selective serotonin re-uptake inhibitors**

The combination of buspirone and selective serotonin reuptake inhibitors (SSRI) was tested in a number of clinical trials on more than 300,000 patients. Although no severe toxicities were observed, there were rare cases of seizures in patients who took buspirone and SSRIs concomitantly.

Separate cases of seizures in patients administered combination therapy with buspirone and SSRIs have been reported from regular clinical use.

Buspirone should be used with caution in combination with serotonergic medicines (including MAOIs, L-tryptophan, triptans, tramadol, buprenorphine, linezolid, SSRIs, lithium and St. John's wort) as there are isolated reports of serotonin syndrome occurring in patients on concomitant SSRI therapy. If this condition is suspected, treatment with buspirone should be immediately discontinued and supportive symptomatic treatment should be initiated.

### **Protein binding**

In vitro buspirone may displace less firmly protein-bound medicines like digoxin. The clinical significance of this property is unknown.

### **Nefazodone**

The co-administration of buspirone (2.5 or 5 mg twice a day) and nefazodone (250 mg twice a day) to healthy volunteers resulted in marked increases in plasma buspirone concentrations (increases up to 20-fold in  $C_{max}$  and up to 50-fold in AUC) and statistically significant decreases (about 50%) in plasma concentrations of buspirone metabolite, 1-pyrimidinylpiperazine, probably due to CYP3A4 inhibition. With 5 mg twice a day doses of buspirone, slight increases in AUC were observed for nefazodone (23%) and its metabolites hydroxynefazodone (HO-EF) (17%) and mCPP (9%). Slight increase in  $C_{max}$  were observed for nefazodone (8%) and its metabolites HO-NEF (11%).

The side effect profile for subjects receiving buspirone 2.5 mg, twice a day and nefazodone 250 mg twice a day was similar to that for subjects receiving either medicine alone. Subjects receiving buspirone 5 mg twice a day and nefazodone 250 mg twice a day experienced side effects such as lightheadedness, asthenia, dizziness and somnolence. It is recommended that the dose of buspirone be lowered when co-administered with nefazodone. Subsequent dose adjustments of either medicine should be based on clinical response.

### **Grapefruit Juice**

In a study in healthy volunteers, co-administration of buspirone (10 mg as a single dose) with double-strength grapefruit juice (200 mL double-strength for 2 days) increased plasma buspirone concentrations (4.3-fold increase in  $C_{max}$  and 9.2-fold increase in AUC). Patients taking Buspirone should avoid consuming large quantities of grapefruit juice.

### **Other inhibitors and inducers of CYP3A4**

When administered with a potent inhibitor of CYP3A4, a low dose of buspirone, used cautiously, is recommended. When used in combination with a potent inducer of CYP3A4 e.g. phenytoin, phenobarbital, carbamazepine, St John's wort an adjustment of the dosage of buspirone may be necessary to maintain buspirone's anxiolytic effect.

### **Fluvoxamine**

In short-term treatment with Fluvoxamine and buspirone double buspirone plasma concentrations are observed compared to mono-therapy by buspirone.

### **Trazodone**

The concomitant use of trazodone hydrochloride and buspirone showed a 3- to 6-fold increase of ALT in some patients.

## **Cimetidine**

Co-administration of buspirone and cimetidine has shown a slight increase in the 1-(2-pyrimidinyl)-piperazine metabolite of buspirone. Because of the high protein binding of buspirone (around 95%) caution is advised when medicines with a high protein binding are given concomitantly.

Baclofen, lofexidine, nabilone, antihistamines may enhance any sedative effect.

## **Effects of buspirone on other medicines**

### **Diazepam**

After addition of buspirone to the diazepam dose regimen, no statistically significant differences in the steady-state pharmacokinetic parameters ( $C_{max}$ , AUC and  $C_{min}$ ) were observed for diazepam, but increases of about 15% were seen for nordiazepam and minor adverse clinical effects (dizziness, headache, and nausea) were observed.

### **Haloperidol**

Concomitant administration of buspirone and haloperidol can increase serum haloperidol concentrations.

### **Digoxin**

In humans, approximately 95% of buspirone is plasma protein bound. *In vitro*, buspirone does not displace tightly bound medicines (i.e. warfarin) from serum proteins. However, *in vitro*, buspirone may displace less firmly protein-bound medicines like digoxin. The clinical significance of this property is unknown.

### **Warfarin**

There are reports on increases in the prothrombin time after the addition of buspirone to a treatment regimen containing warfarin.

### **Other CNS depressants**

The sedative effect of buspirone may be enhanced if taken with other CNS depressants. Therefore, the concomitant use of buspirone with CNS depressant medicines should be monitored carefully.

### **Alcohol**

The sedative effects of buspirone may be enhanced if taken with alcohol. Therefore the concurrent consumption of alcohol should be avoided.

## **4.6 Fertility, pregnancy and lactation**

### **Pregnancy**

Category B1.

In some animal studies, large doses of buspirone during pregnancy had adverse effects on survival and on birth and weaning weight, although there was no effect on foetal development. Since the relevance of this finding in humans has not been established, buspirone should be used only if clearly needed during pregnancy.

### **Breast-feeding**

Available toxicological data in animals have shown excretion of buspirone (metabolite) in milk (for details see section 5.3). A risk to the suckling child cannot be excluded. Lactation should therefore be discontinued during the treatment with buspirone.

### **Labour and delivery**

The effect of buspirone on labour and delivery in women is unknown.

## **Fertility**

No data available. For pre-clinical fertility data refer to section 5.3.

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

It cannot be excluded that buspirone – especially at the beginning of treatment and after a change in dose – but also by normal use affects the capacity of reaction to such extent that it has influence on the ability to drive and use machines.

Studies have shown that buspirone has less sedative effect than other anxiolytics, as it produces no significant psychomotor impairment. However, its effects on the individual patient's central nervous system are not predictable. Therefore, patients should be warned not to drive or to operate complex machinery until they are relatively sure that their performance is unimpaired by the use of buspirone.

### **4.8 Undesirable effects**

The following frequency categories are used for classification of adverse reactions:

Very common ( $\geq 1/10$ )

Common ( $\geq 1/100$  to  $< 1/10$ )

Uncommon ( $\geq 1/1,000$  to  $< 1/100$ )

Rare ( $\geq 1/10,000$  to  $< 1/1,000$ )

Very rare ( $< 1/10,000$ )

Not known (cannot be estimated from the available data)

### **Blood and lymphatic system disorders**

Rare: blood count changes (eosinophilia, leukopenia, thrombocytopenia), bleeding disorders

### **Immune system disorders**

Rare: allergic reactions

### **Endocrine disorders**

Rare: thyroid dysfunction

### **Metabolism and nutrition disorders**

Uncommon: increased appetite, anorexia, weight gain, weight loss

### **Psychiatric disorders**

Common: nightmares, insomnia, nervousness, agitation, anger, hostility, confusion, depression

Uncommon: depersonalisation, euphoria, dysphoria, urge to move, anxiety, loss of interest, association disturbances, hallucinations, suicidal thoughts

Rare: mood swings, claustrophobia, psychosis, alcohol abuse

## **Nervous system disorders**

Common: headache, drowsiness, dizziness, light-headedness, impaired concentration

Uncommon: numbness, abnormal sensations (e.g. tingling, pricking sensation), loss of coordination, tremors, seizures, roaring in the head, altered taste, drooling

Rare: extrapyramidal symptoms including early and late dyskinesia, dystonia and rigidity, parkinsonism, akathisia, restless legs syndrome, slowed reaction time, involuntary movements, stupor, slurred speech, transient memory gaps, serotonin syndrome, loss of voice

## **Eye disorders**

Common: blurred vision

Uncommon: redness of the eyes, itchy eyes, conjunctivitis

Rare: eye pain, photophobia, sensation of pressure on the eyes, tunnel vision

## **Ear and labyrinth disorders**

Common: tinnitus

Uncommon: hyperacusis

## **Cardiac disorders**

Common: nonspecific chest pain

Uncommon: tachycardia/palpitations

Rare: heart failure, heart attack, cardiomyopathy, bradycardia

## **Vascular disorders**

Uncommon: brief episodes of fainting, hypo- or hypertension

Rare: cerebral blood flow disorders

## **Respiratory, thoracic and mediastinal disorders**

Common: sore throat, stuffy nose

Uncommon: significantly increased breathing frequency, shortness of breath, chest pressure, altered sense of smell

Rare: nosebleeds

## **Gastrointestinal disorders**

Common: nausea, dry mouth, gastrointestinal symptoms, diarrhoea

Uncommon: rectal bleeding, constipation, flatulence, irritable colon, vomiting

Rare: burning tongue, hiccups

## **Hepatobiliary disorders**

Uncommon: increased liver enzymes



### **Skin and subcutaneous tissue disorders**

Uncommon: urticaria, flushing, tendency to bruising, hair loss, dry skin, eczema, vesicula

Rare: small haemorrhages of the skin, acne, nail thinning

### **Musculoskeletal and connective tissue disorders**

Uncommon: muscle cramps, muscle pain, muscle tension, joint pain

Rare: muscle weakness

### **Renal and urinary disorders**

Uncommon: lower urinary tract symptoms

Rare: enuresis, nocturia

### **Reproductive system and breast disorders**

Uncommon: menstrual disorders, decreased or increased libido

Rare: amenorrhea, pelvic inflammatory disease, abnormal ejaculation, impotence, galactorrhoea, gynaecomastia

### **General disorders and administration site conditions**

Common: weakness

Uncommon: fever, malaise, fatigue, sweating, clammy hands, oedema, facial oedema

Rare: cold intolerance

### **Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>.

## **4.9 Overdose**

### **Signs and symptoms**

Mainly the following symptoms have been observed: nausea, vomiting, dizziness, fatigue, pupillary constriction and stomach complaints. Even with daily doses of up to 2,400 mg in humans, no serious complications were observed.

### **Treatment**

Treatment should be symptomatic and supportive. The benefit of gastric decontamination is uncertain. Administration of activated charcoal can be considered. As in any other cases of an overdose, breathing, pulse and blood pressure should be monitored. A specific antidote is not known. Buspirone is not removed by haemodialysis, the metabolite 1-PP is partially removed by haemodialysis.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

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## 5. Pharmacological Properties

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### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Psycholeptics; azaspirodecandione derivatives.

ATC code: N05BE01

Buspirone hydrochloride belongs chemically to the class of pharmacologic agents with selective anxiolytic psychotropic activity known as the azapirones.

#### Mechanism of action

Buspirone represents the first anxiolytic of the class of active substances known as azaspirones. These are neither chemically nor pharmacologically related to benzodiazepines, barbiturates, or other psychotropic substances.

Buspirone is a complete agonist at presynaptic 5-hydroxytryptamine type 1A receptors and a partial agonist at postsynaptic 5-hydroxytryptamine type 1A receptors in the CNS.

Apparently, the adaptive modulations of 5-HT neurotransmission play a key role in the anxiolytic effects of buspirone after repeated administration, which is why there is a delayed onset of action of 2–4 weeks.

The buspirone metabolite 1-[2-pyrimidinyl]-piperazine (1-PP) is a potent  $\alpha_2$ -antagonist, and as such it has an impact on the noradrenergic system, which can be associated with psychostimulatory and antidepressive effects.

The prevention of or dealing with stress-induced behavioural disorders may perhaps be considered as the fundamental characteristic of buspirone and other 5-HT<sub>1A</sub> agonists. In a number of preclinical studies, buspirone had properties that are characteristic of anxiolytics and antidepressants.

Buspirone or 1-PP do not interact with the GABA-benzodiazepine receptor complex. In contrast to benzodiazepines, buspirone showed no signs of hypnotic-sedative, muscle relaxant, anticonvulsant, or alcohol abusive/addictive effects. In contrast to benzodiazepines, it is unlikely that withdrawal symptoms or a rapid rebound of anxiety symptoms will occur after discontinuation of buspirone.

#### Paediatric population

Placebo-controlled trials, in which 334 patients were treated with buspirone for up to six weeks, have not shown buspirone at doses recommended for adults to be an effective treatment for generalised anxiety disorder in patients less than 18 years.

### 5.2 Pharmacokinetic properties

#### Absorption

Buspirone is rapidly absorbed in humans following oral administration, however, the medicine undergoes extensive first pass metabolism with only 4% of the dose reaching systemic circulation. Peak plasma levels are attained after 60 to 90 minutes; they were found to be a linear function of the administration dose over the entire therapeutic range.

#### Distribution

The plasma half-life is 2–3 hours. In plasma, more than 95% of the active ingredient is protein bound. Other medicines with high protein binding in blood, such as phenytoin, propranolol and warfarin, are not displaced by buspirone from plasma proteins *in vitro* at clinically relevant buspirone concentrations. At higher concentrations, digoxin is displaced by buspirone *in vitro*; however, the clinical relevance of this finding is not clear.

## **Biotransformation**

Buspirone is metabolised primarily by oxidation; the involvement of cytochrome P450 3A4 (CYP3A4) was demonstrated *in vitro*. Several hydroxylated derivatives and two pharmacologically active metabolites, 6-hydroxybuspirone (6-OHB) and 1-pyrimidinylpiperazine (1-PP) are produced.

In an animal study investigating the anxiolytic potential, 6-OHB displayed the same activity profile as buspirone.

In healthy volunteers, who received buspirone orally, the plasma concentrations of 6-OHB were approximately 40 times greater than those of buspirone, which leads to the suggestion that mainly this metabolite contributes to the clinical anxiolytic effects.

In animal studies, that have led to the conclusion of anxiolytic potential, the activity of 1-PP is approximately 25% or less compared to the activity of buspirone.

## **Elimination**

The excretion of buspirone and its metabolites is approximately 29 to 63% of the dose was excreted in the urine and 18 to 38% in faeces. The elimination of buspirone is reduced in patients with impaired hepatic or renal function. There were no significant differences in the pharmacokinetics of buspirone in relation to age or gender.

## **Renal impairment**

After a single administration to patients with renal insufficiency (creatinin clearance 20– 49 mL/min/1.72 m<sup>2</sup>) a slight increase in the buspirone blood levels was seen, without increase of the half-life time. A single administration to anuric patients causes an increase in the blood levels of the metabolite 1-pyrimidine/piperazine (1-PP), in which dialysis did not prove to have any influence on the buspirone levels, neither on the 1-PP levels.

## **Hepatic impairment**

As may be expected agents as buspirone used in patients with a reduced liver function show a reduced “first-pass effect”. After a single administration to patients with liver cirrhosis, higher maximum concentrations of unchanged buspirone are seen, with an increase in the half life time.

## **Paediatric population**

Plasma concentrations of buspirone and its active metabolite were higher in paediatric patients, compared to adults given equivalent doses.

## **5.3 Preclinical safety data**

In studies with different animal species, a moderate acute toxicity of buspirone hydrochloride was determined. LD<sub>50</sub> after oral treatment was 330–660 mg/kg BW in rats, 200–420 mg/kg BW in mice, about 300 mg/kg BW in dogs, and about 350 mg/kg BW in monkeys. Death mostly occurred immediately after administration of the medicine and was accompanied by tonic-clonic seizures, body stiffness and other signs of CNS toxicity.

Studies of toxicity after repeated oral administration of buspirone hydrochloride in rats (up to 160 mg/kg BW/d) and mice (up to 200 mg/kg BW/day) showed dose-related weight loss. Tremor, hyperventilation and tachycardia were occasionally seen in rats, and amyloid deposits in the kidneys and the testicular tissue (ranging to testicular atrophy) and in the gastrointestinal tract were seen in mice.

After repeated oral administration of buspirone in monkeys, a dose-dependent mortality (> 50% at 100 mg/kg BW/day buspirone hydrochloride) and CNS toxicity was reported, including tremors, hypoactivity, catatonia, sedation and abnormal chewing movements.

Organ-specific toxic changes were not observed.

Reproductive toxicity studies in rats and rabbits revealed no evidence of teratogenic or fetotoxic effects of buspirone. In lactating rats, buspirone (metabolite) was excreted in the

In *in vitro* and *in vivo* studies, buspirone showed no mutagenic or genotoxic effects.

Long-term studies showed no evidence of carcinogenic effects when buspirone hydrochloride was given to rats (up to 160 mg/kg BW/day for 2 years) and mice (up to 200 mg/kg BW/day for 18 months).

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## 6. Pharmaceutical Particulars

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### 6.1 *List of excipients*

BUSPIRONE VIATRIS tablet also contains:

- lactose monohydrate
- microcrystalline cellulose
- sodium starch glycollate
- colloidal silicon dioxide
- magnesium stearate.

Contains sugars as lactose

### 6.2 *Incompatibilities*

Not applicable.

### 6.3 *Shelf life*

3 years.

### 6.4 *Special precautions for storage*

Store at or below 25°C. Protect from light.

### 6.5 *Nature and contents of container*

HDPE bottle with PP lid. Pack size of 100 tablets

Al/PVC blister packs of 30 or 100 tablets

Al/PVC/PVdC blister packs of 30 or 100 tablets

Not all pack types and sizes may be marketed.

### 6.6 *Special precautions for disposal*

Not applicable.

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## 7. Medicines Schedule

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Prescription Medicine

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## 8. Sponsor Details

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Viatrix Ltd  
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## 9. Date of First Approval

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4 July 2002

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## 10. Date of Revision of the Text

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03 March 2023

### ***Summary table of changes***

Section	Summary of new information
3	Minor editorial update to clarify the appearance of the 10 mg tablet
10	New date for revision of text