SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Hydroxyzine hydrochloride 25 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 mg film-coated tablet contains 10 mg hydroxyzine hydrochloride.
Each 25 mg film-coated tablet contains 10 mg hydroxyzine hydrochloride.

Excipient with known effect:
10 mg 22 mg lactose (as lactose monohydrate).
25 mg: 55 mg lactose (as lactose monohydrate).

For the full list of excipients, see section 6.1.

3 **PHARMACEUTICAL** FORM

Film-coated tablet.

10 mg: White to off-white, 5.0 mm round shaped, biconvex, film coated tablets.

25 mg: White to off-white, 10.0 mm x 4.0 mm caplet shaped, biconvex, film coated tablets with score line on both sides. The tablet can be divided into two equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of anxiety in adults.
Symptomatic treatment of pruritus in adults and children ≥ 6 years of age.

4.2 Posology and method of administration

Posology
Hydroxyzine Hydrochloride should be used at the lowest effective dose and for the shortest possible duration.

Adults:

Symptomatic treatment of anxiety:

50 mg daily, divided into 3 doses daily, with 12.5 mg, 12.5 mg, 25 mg, where the larger dose can be taken in the evening. In more severe cases, doses up to 100 mg/day can be used The maximum daily dose is 100 mg per day.

Medicinal treatment of anxiety should always be used as adjuvant therapy. As far as possible, treatment should be initiated, supervised and discontinued by the same physician.

Symptomatic treatment of pruritus:

The starting dose is 25 mg in the evening (about an hour before bedtime), then if necessary up to 25 mg in total 3-4 times per day. The maximum daily dose is 100 mg per day.

Children aged ≥6–17 years:

Symptomatic treatment of pruritus:

1 mg/kg/day up to 2 mg/kg/day in divided doses (see 5.2).
In children <40 kg, the maximum daily dose is 2 mg/kg/day.
In children ≥40 kg, the maximum daily dose is 100 mg per day.
Dose adjustment
Dose should be adjusted within the given dose range in accordance with the treatment response in the patient.

Special populations

Elderly:
In the elderly, it is advised to start with half the recommended dose due to the prolonged action. The lowest possible dose should be selected in the treatment of elderly patients. The maximum daily dose in elderly is 50 mg/day (see section 4.4). The results and need for treatment should be continuously assessed.

Patients with renal impairment:
Caution is recommended in patients with impaired renal function. Dose should be reduced in patients with moderate or severe renal impairment due to decreased excretion of its metabolite cetirizine. See the following table and adjust the dose as directed. The anxiolytic effect mediated by hydroxyzine may be affected by dose reduction and this should be evaluated on an individual basis.

Dose adjustment for adult patients with impaired renal function.

Group	eGFR (ml/min)	Percentage of recommended dose
Mild renal impairment	60 - < 90	100%
Moderately impaired renal function	30 - < 60	50%
Severe renal impairment	15 - < 30	25%
End stage renal failure (ESRD)	< 15	25% 3 times a week

Patients with hepatic impairment:
Caution is required in patients with hepatic impairment, and a reduction of the dose should be considered.

Paediatric population:
Hydroxyzine Bluefish film-coated tablets are not recommended in paediatric patients under the age of 6 years as they may have difficulty swallowing tablets.

The safety and efficacy of hydroxyzine in children under 12 months of age have not yet been established. No data are available.

Method of administration:
The tablets should be swallowed with a sufficient amount of water. The tablets can be taken with or without food.

4.3 Contraindications

- Hypersensitivity to the active substance, to cetirizine, to other piperazine derivatives, aminophylline, ethylenediamine or any of the excipients listed in section 6.1.
- Patients with porphyria.
- Pregnancy and breast-feeding (see section 4.6).
- Patients with a known acquired or congenital QT interval prolongation.
- Patients with a known risk factor to QT interval prolongation including a known cardiovascular disease, significant electrolytes imbalance (hypokalaemia, hypomagnesaemia), family history of sudden cardiac death, significant bradycardia, concomitant use with drugs known to prolong the QT interval and/or induce Torsade de Pointes (see sections 4.4 and 4.5).

4.4 Special warnings and precautions for use

Cardiovascular effects
Hydroxyzine has been associated with prolongation of the QT interval on the electrocardiogram. During post-marketing surveillance, there have been cases of QT interval prolongation and torsade de pointes in patients taking hydroxyzine. Most of these patients had other risk factors, electrolyte abnormalities and concomitant treatment that may have been contributory (see section 4.8). Hydroxyzine should be used at the lowest effective dose and for the shortest possible duration.

Treatment with hydroxyzine should be stopped if signs or symptoms occur that may be associated with cardiac arrhythmia, and the patients should seek immediate medical attention.

Patients should be advised to promptly report any cardiac symptoms.

Patients with hepatic impairment
Dosage should be reduced for patients with hepatic impairment (see section 4.2).
In patients with hepatic impairment who receive hydroxyzine regularly, liver function should be monitored.

Patients with renal impairment
Hydroxyzine should be used with caution in patients with moderate and severe renal impairment and the dose should be reduced (see section 4.2).

Elderly patients
Hydroxyzine is not recommended in elderly patients because of a decrease of hydroxyzine elimination in this population as compared to adults and the greater risk of adverse reactions (e.g. anticholinergic effects) (see sections 4.2 and 4.8).
In elderly patients, it is recommended to begin treatment with half of the recommended dose due to prolonged action (see section 4.2).

Other warnings and precautions for use

Because of its potential anticholinergic effects, Hydroxyzine should be used with caution in in patients suffering from glaucoma, urinary tract obstruction, decreased gastro-intestinal motility, myasthenia gravis, or dementia.

Hydroxyzine should be administered cautiously in patients with increased risk of convulsions.

Younger children are more susceptible to develop adverse events related to the central nervous system (see section 4.8). In children, convulsions have been more frequently reported than in adults.

Dosage adjustments may be required if hydroxyzine is used concomitantly with other central nervous system depressant drugs or drugs with anticholinergic properties (see section 4.5).

Concomitant use of alcohol and hydroxyzine should be avoided (see section 4.5).

The treatment should be stopped at least 5 days before allergy testing or methacholine bronchial challenge to avoid effects on the test results (see section 4.5).

Dry mouth may occur with high doses and patients should therefore be informed about this risk and observe good mouth and tooth hygiene.

The prescriber should discuss the anticipated duration of treatment with the patient and inform about the initial adverse reactions.
Cerebrovascular effects

An about 3-fold risk of cerebrovascular events has been observed in randomised, placebo-controlled clinical studies with certain atypical neuroleptics in patients with dementia. Background mechanism for this increased risk is not known. An increased risk with other neuroleptics and in other patient populations cannot be excluded. Therefore, hydroxyzine should be used with caution in patients with risk factors for stroke.

Excipients

Hydroxyzine film-coated tablets contain lactose (see section 6.1).

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Hydroxyzine film-coated tablets contain sodium
This medicine contains less than 1 mmol sodium (23 mg) per 10 mg tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Associations contraindicated:
Co-administration of hydroxyzine with drugs known to prolong the QT interval and/or induce Torsade de Pointes e.g. class IA (e.g. quinidine, disopyramide) and III antiarrhythmics (e.g. amiodarone, sotalol), some antihistamines, some antipsychotics (e.g. haloperidol), some antidepressants (e.g. citalopram, escitalopram), some antimalarial drugs (e.g. mefloquine), some antibiotics (e.g. erythromycin, levofloxacin, moxifloxacin), some antifungal agents (e.g. pentamidine), some gastro-intestinal medicines (e.g. prucalopride), some medicines used in cancer (e.g., toremifene, vandetanib), methadone, increase the risk of cardiac arrhythmia. Therefore, the combination is contra-indicated (see section 4.3).

Associations not recommended:

Betahistine and anticholinesterase drugs
Hydroxyzine antagonises the effects of betahistine and of anticholinesterases.

Allergy testing
The treatment should be stopped at least 5 days before allergy testing or methacholine bronchial challenge, to avoid effects on the test results.

MAO-inhibitors
Simultaneous administration of hydroxyzine with monoamine oxidase inhibitors should be avoided.

Associations requiring precaution of use:

Bradycardia and hypokalaemia-inducing drugs
Caution with bradycardia and hypokalaemia-inducing drugs.

CNS depressants
Patients should be informed that hydroxyzine may potentiate the effects of CNS depressants or active substances having anticholinergic properties. Dose should be adapted on an individual basis.

Alcohol
Alcohol potentiates the effects of hydroxyzine.

Adrenaline
Hydroxyzine counteracts the adrenaline pressor action of adrenaline (see 4.9).

Phenytoin
In rats, hydroxyzine antagonised the anticonvulsant action of phenytoin.

Cimetidine
Cimetidine 600 mg twice daily has been shown to increase the serum concentrations of hydroxyzine by 36% and to decrease peak concentrations of the metabolite cetirizine by 20%.

CYP2D6 substrates
Hydroxyzine is an inhibitor of CYP2D6 (Ki: 3.9 µM: 1.7 µg/ml) and may at high doses cause drug interactions with CYP2D6 substrates:
- beta-blockers (metoprolol, propafenone, timolol)
- SSRIs (fluoxetine, fluvoxamine)
- antidepressants (amitriptyline, clomipramine, desipramine, duloxetine, imipramine, paroxetine, venlafaxine)
- antipsychotics (aripiprazole, haloperidol, risperidone, thioridazine),
- codeine, dextromethorphan, flecainide, mexiletine, ondansetron, tamoxifen, tramadol.

UDP-glucuronyl transferase and cytochrome P450
Hydroxyzine is unlikely to impair the metabolism of drugs which are substrates for cytochrome P450 2C9, 2C19 and 3A4 and UDP-glucuronyl transferases.

CYP3A4/5 inhibitors
Hydroxyzine is metabolised by alcohol dehydrogenase and CYP3A4/5 and an increase in hydroxyzine blood concentrations may be expected when hydroxyzine is co-administered with active substances known to be potent inhibitors of these enzymes. Examples of potent inhibitors of CYP3A4/5 are telithromycin, clarithromycin, delavirdine, stiripentol, ketoconazole, voriconazole, itraconazole, posaconazole and certain HIV protease inhibitors, including atazanavir, indinavir, nelfinavir, ritonavir, saquinavir, lopinavir/ritonavir, saquinavir/ritonavir, and tipranavir/ritonavir and examples of potent inhibitors of alcohol dehydrogenase are disulfiram and metronidazole. No interaction with CYP3A4/5-substrate is expected with hydroxyzine.

Thiazide diuretics
Simultaneous use of active substances that may cause electrolyte disturbances, such as thiazide diuretics (hypokalaemia), should be avoided as they increase the risk of malignant arrhythmias (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of reliable data on the use of hydroxyzine in pregnant women. Hydroxyzine crosses the placental barrier leading to higher foetal than maternal concentrations. Animal studies have shown reproductive toxicity (see section 5.3). Therefore, Hydroxyzine Hydrochloride is contraindicated during pregnancy.

In neonates whose mothers received hydroxyzine during late pregnancy and/orlabour, the following events were observed immediately or only a few hours after birth: hypotonia, movement disorders including extrapyramidal disorder, clonic movements, CNS depression, neonatal hypoxic conditions or urinary retention.

Breast-feeding
Cetirizine, the main metabolite of hydroxyzine, is excreted in human milk. Although no formal studies have been conducted concerning the excretion of hydroxyzine in human milk, serious undesirable effects have been seen in breast-fed newborns/infants of hydroxyzine-treated women. Therefore, hydroxyzine is contraindicated during breast-feeding. Brest-feeding must be discontinued if hydroxyzine treatment is necessary.

4.7 Effects on ability to drive and use machines

Hydroxyzine Hydrochloride may impair the ability to react and to concentrate. Patients should be warned of this possibility and cautioned against driving a car or operating machinery. Concomitant use of hydroxyzine with alcohol or other sedative drugs should be avoided as it aggravates these effects.

4.8 Undesirable effects

The most common undesirable effect of the sedating antihistamines is CNS depression. Effects vary from slight drowsiness to deep sleep, and include lassitude, dizziness, and incoordination. Paradoxical stimulation may occasionally occur, especially at high doses and in children and the elderly. If sedative effects occur, they may diminish after a few days of treatment. Other common adverse effects include anti-cholinergic activity, hypersensitivity reactions, headache, psychomotor impairment and antimuscarinic effects.

A Clinical trials

Oral administration of hydroxyzine:

The following table lists the undesirable effects reported in placebo-controlled clinical trials at a rate of at least 1% for hydroxyzine. The trials included 735 patients who received hydroxyzine up to 50 mg daily and 630 patients who received placebo.

Undesirable effect (PT)	undesirable effects for hydroxyzine, %	undesirable effects for placebo, %
Sleepiness	13.74	2.70
Headache	1.63	1.90
Tiredness	1.36	0.63
Dry mouth	1.22	0.63

B Post-marketing experience

The table below lists, per system organ class and frequency, the undesirable effects reported during post-marketing use of the drug.

The frequency has been estimated using the following definitions:

very common (≥1/10); common (≥1/100 to < 1/10); uncommon (≥1/1,000 to <1/100); rare (≥ 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:

Not known: thrombocytopenia

Immune system disorders:

Rare: hypersensitivity reactions

Very rare: anaphylactic shock

Psychiatric disorders:

Uncommon: agitation, confusion

Rare: disorientation, hallucination

Not known: aggression, depression, tics

Nervous system disorders:

Common: sedation

Uncommon: dizziness, insomnia, tremor

Rare: Seizures, dyskinesia

Not known: dystonia, paraesthesia

Eye disorders:

Rare: accommodation disorder, blurred vision

Not known: oculogyric crisis

Cardiac disorders:

Rare: cardiac arrest, ventricular fibrillation, ventricular tachycardia

Not known: ventricular arrhythmias (e.g. Torsade de Pointes), QT interval prolongation (see section 4.4).

Vascular disorders:

Rare: hypotension

Respiratory, thoracic and mediastinal disorders:

Very rare: bronchospasm

Gastrointestinal disorders:

Uncommon: nausea

Rare: constipation, vomiting

Not known: diarrhoea

Hepatobiliary disorders:

Rare: liver function tests abnormal

Not known: hepatitis

Skin and subcutaneous tissue disorders:

Rare: pruritis, erythema, papular rash, urticaria, dermatitis

Very rare: angioedema, increased sweating, fixed drug eruption, acute generalized exanthematous pustulosis (AGEP), erythema multiforme, Stevens-Johnson syndrome

Renal and urinary disorders:

Rare: urinary retention

Not known: dysuria, enuresis

General disorders and administration site conditions:

Uncommon: malaise, pyrexia

Not known: asthenia, oedema

Investigations:

Not known: weight increased

Treatment with neuroleptics may cause prolongation of the QT interval and cardiac arrhythmias. Cases of sudden death which may have cardiac causes (see section 4.4) have been reported during treatment with these drugs.

Paediatric population and elderly

Children and elderly are more susceptible to side effects.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Toxicity:
60-100 mg hydroxyzine given to a 2 year old child resulted in no or mild intoxication, 300 mg hydroxyzine given to a 2 year old child resulted in severe intoxication. 1-1.5 g hydroxyzine given to adults resulted in mild intoxication. 1.5-2.5 g hydroxyzine given to adults resulted in moderate intoxication.

Symptoms:
Symptoms observed after a major overdose are mainly associated with strong anticholinergic effects, CNS depression or CNS paradoxical stimulation. The symptoms include nausea, vomiting, tachycardia, pyrexia, somnolence, impaired pupillary reflex, tremor, confusion, or hallucination. These may be followed by depressed level of consciousness, respiratory depression, convulsions or hypotension.

Deepening coma and cardiorespiratory collapse may ensue. Prolonged QT interval and serious arrhythmia with fatal outcomes have been described in connection with an overdose of neuroleptics.

Treatment:
Symptomatic and supportive treatment is indicated. Gastric lavage with endotracheal intubation may be performed if a clinically significant amount of medicine has been ingested. Activated charcoal should be considered, but there is few data that supports the effect. There is no specific antidote. Airways, respiratory and circulatory status must be closely monitored with continuous ECG recordings and adequate oxygen supply must be available. Monitoring of heart rate and blood pressure must be done until the patient is free of symptoms for 24 hours.

Patients with changes in mental status should be examined to determine simultaneous use of other drugs or alcohol, and be given oxygen, naloxone, glucose and thiamine, if needed.

Noradrenalin or metaraminol should be administered when a need for a blood pressure stimulant exists.

Adrenaline must not be used in the treatment of intoxication since it could decrease blood pressure even further.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Psycholeptics, anxiolytica, diphenylmethane derivatives, ATC code: N05BB01

The active substance, hydroxyzine hydrochloride, is a diphenylmethane derivative, which does not belong to the same chemical group as phenothiazines, reserpine, meprobamate and benzodiazepines.

Mechanism of action
Hydroxyzine hydrochloride is not a cortical depressant, but its effect may be due to CNS suppression of the activity of certain key subcortical areas.

Pharmacodynamic effects, clinical efficacy and safety
Hydroxyzine hydrochloride has been experimentally found to have antihistaminic and bronchodilatory effects and the effects are confirmed clinically. In addition, an anti-emetic effect has been demonstrated in both the apomorphine test and the veriloid test. Pharmacological and clinical studies indicate that hydroxyzine hydrochloride in therapeutic dose does not increase gastric secretion or acidity and in most cases provides mild antisecretory benefits. Healthy volunteer adults' and children's hives and reddening has been shown to decrease when the skin is first injected with histamine or antigens. Hydroxyzine hydrochloride has also proven effective in reducing itching for various types of urticaria, eczema and dermatitis.

In the case of hepatic failure, the effect of one dose of antihistamine can last as long as 96 hours after dosing.

EEG studies conducted in healthy volunteers have shown that the medicinal product has an anxiolytic-sedative profile. An anxiolytic effect was confirmed by a variety of classical psycho-metric

tests. It was found in polygraphic sleep studies on patients suffering from anxiety and insomnia that the total duration of sleep was increased, total time of nocturnal wakeups decreased, and the time to go to sleep was reduced, after both the 50 mg single dose and repeated dosing. Muscle tension was found to decrease in over-anxious patients using a daily dose of 3 x 50 mg.
Memory disturbances were not observed. Patients with anxiety did not show any symptoms of withdrawal after 4 weeks of treatment.

Onset of action
Antihistaminic effect begins about 1 hour after an oral dose. Sedative effect begins 30–45 minutes after taking a tablet. Hydroxyzine hydrochloride also has a sympatolytic and spasmolytic effect. Its affinity for muscarinic receptors is low. Hydroxyzine hydrochloride has low analgesic effect.

Paediatric population
The pharmacokinetics and antipruritic effects of hydroxyzine hydrochloride were studied in 12 children (mean age 6.1 ± 4.6 years) with severe atopic dermatitis, each given a single 0.7 mg/kg oral dose. Pruritis was significantly suppressed from 1 to 24 hours after the administration of the dose, with greater than 85 % suppression from 2 to 12 hours. The potent antipruritic effect persists even when serum concentrations of the active substance are low (only 10% of the maximum levels achieved). In children, the biological effects of hydroxyzine hydrochloride appear to be much more prolonged than would be predicted from the half-life values

5.2 Pharmacokinetic properties

Absorption
Hydroxyzine hydrochloride is rapidly absorbed from the gastrointestinal tract. Maximum plasma concentration (Cmax) has been shown to occur after around 2 hours (t_{max}) after oral administration. After single doses of 25 mg and 50 mg in adults, C_{max} is normally 30 respective 70 ng/ml. Rate and extent of exposure to hydroxyzine hydrochloride are about the same as if given as a tablet or syrup. After repeated once daily dosing, the concentration increases about 30%. Oral bioavailability of hydroxyzine hydrochloride compared with intramuscular (IM) administration is about 80%.

Distribution
Hydroxyzine hydrochloride is widely distributed in the body and is generally more concentrated in tissues than in plasma. The apparent volume of distribution is 7-16 l/kg in adults. Hydroxyzine hydrochloride is taken up in the skin after oral administration. The hydroxyzine concentrations in the skin are higher than serum concentrations after both single and multiple dose administration. Hydroxyzine hydrochloride crosses the blood-brain and placental barrier which may lead to higher foetal than maternal concentrations.

Biotransformation
Hydroxyzine hydrochloride is extensively metabolized. The formation of the main metabolite cetirizine, a carboxylic acid metabolite (approximately 45% of the oral dose), is mediated by alcohol dehydrogenase. This metabolite has significant peripheral H_1-antagonistic properties. Other identified metabolites include an N-dealkylated metabolite, and an O-dealkylated metabolite with a plasma half-life of 59 hours. These metabolic pathways are mediated primarily by CYP3A4/5.

Elimination
Hydroxyzine's half-life in adults is about 14 hours (7-20 h). Half-life of the main metabolite cetirizine in adults is approximately 10 hours. Plasma clearance (CL/F) calculated after an oral dose from studies, is 13 ml/min/kg. Only 0.8 % of the dose is excreted unchanged in urine after an oral dose. Cetirizine is mainly excreted unchanged in urine (25 % of oral hydroxyzine hydrochloride dose).

Special populations

Elderly
Hydroxyzine's pharmacokinetics in elderly was investigated in 9 healthy elderly subjects (69.5 ± 3.7 years) after a single dose of 0.7 mg/kg. Hydroxyzine's half-life increased to 29 hours and the apparent volume of distribution volume rose to 22.5 l/kg. Reduction of daily dose is recommended in elderly patients (see section 4.2).

Paediatric population
Hydroxyzine's pharmacokinetics was evaluated in 12 children (6.1 ± 4.6 years; 22.0 ± 12.0 kg) after an oral dose of 0.7 mg/kg. Oral plasma clearance per kg was about 2.5 times higher than in adults. The half-life was shorter than in adults. It was about 4 hours in 1 year old infants and 11 hours in 14 year old adolescents and increases with age. Dosage should be adjusted to the child (see section 4.2).

Hepatic impairment
In subjects with hepatic impairment secondary to primary biliary cirrhosis, plasma clearance (CL/F) was approximately 66 % of that in normal subjects. Half-life was increased to 37 hours and serum concentrations of the carboxylic acid metabolite cetirizine were higher than in young subjects with normal hepatic function.

Renal impairment
Hydroxyzine's pharmacokinetics was studied in 8 subjects with severe renal impairment (creatinine clearance 24 ± 7 ml/min). The exposure (AUC) of hydroxyzine hydrochloride did not change significantly, while it increased about 5 times for the carboxylic acid metabolite cetirizine. This metabolite was not removed efficiently by dialysis. To avoid significant accumulation of cetirizine after repeated dose of hydroxyzine hydrochloride, the daily dose of hydroxyzine hydrochloride should be reduced in patients with renal impairment (see section 4.2).

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and genotoxicity. No animal carcinogenicity studies have been performed with hydroxyzine.

In rats and rabbits, foetal malformations and foetal abortions were seen with hydroxyzine doses of 50 mg/kg.

In isolated canine Purkinje fibres, hydroxyzine at concentrations of 3 µM increased action potential duration suggesting that there was an interaction with potassium channels involved with the repolarisation phase. At higher concentrations, 30 µM, there was a marked decrease in the action potential duration suggesting a possible interaction with calcium and/or sodium currents. Hydroxyzine produced inhibition of the potassium (IKr) current in hERG channels expressed in mammalian cells, with an IC50 of 0.62 µM, a concentration that is between 10 and 60-fold higher than therapeutic concentrations. However, the hydroxyzine concentrations required to produce effects on cardiac electrophysiology are 10 to 100-fold higher than those required to block H1 and 5-HT2 receptors. In unrestrained conscious dogs monitored by telemetry, hydroxyzine and its enantiomers produced similar cardiovascular profiles though there were some minor differences. In the first dog telemetry study, hydroxyzine (21 mg/kg orally) slightly increased heart rate and shortened PR and QT intervals. There was no effect on QRS and QTc intervals, and thus at normal therapeutic doses, these slight changes are unlikely to be of clinical relevance.

Similar effects on heart rate and PR interval were observed in a second dog telemetry study, where the absence of effects of hydroxyzine on QTc interval was confirmed up to a single oral dose of 36 mg/kg.

6.1 List of excipients

Tablet core:

Cellulose microcrystalline

Lactose monohydrate

Croscarmellose sodium

Silica, colloidal anhydrous

Talc

Magnesium stearate

Coating:

Hypromellose 5cPs

Macrogol 400

Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 Years

6.4 Special precautions for storage

PVC/PVdC- Alu blister:

This medicinal product does not require any special temperature storage conditions.

HDPE bottle:

This medicinal product does not require any special temperature storage conditions.

Keep the bottle tightly closed in order to protect from moisture.

6.5 Nature and contents of container

The film-coated tablets are supplied in PVC/PVdC - Alu blisters & HDPE bottles.

PVC/PVdC- Alu blister:
10 mg: 25, 30, 84, 100 and 250 tablets25 mg: 20, 25, 28, 30, 50, 60, 100 and 250 tablets.

HDPE bottle with Polypropylene child resistant cap with liner and silica gel desiccant:
10 mg: 25, 30, 84 and 100 tablets
25 mg: 20, 25, 28, 30, 50, 60 and 100 tablets.

HDPE bottle with Polypropylene cap with liner and silica gel desiccant:
250 tablets. This pack is for dose-dispensing.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Bluefish Pharmaceuticals AB
Gävlegatan 22
113 30 Stockholm
Sweden

8 MARKETING AUTHORISATION NUMBER(S)

Hydroxyzine Hydrochloride 10 mg film-coated tablets PL 31774/0048
Hydroxyzine Hydrochloride 25 mg film-coated tablets PL 31774/0049

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27/04/2022

10 DATE OF REVISION OF THE TEXT

11/10/2024