Voxyzine Hydroxyzine HCl Film Coated Tablet

1 NAME OF THE MEDICINAL PRODUCT

Voxyzine Hydroxyzine HCl Film Coated Tablet 10 mg
Voxyzine Hydroxyzine HCl Film Coated Tablet 25 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

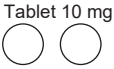
Voxyzine Hydroxyzine HCl Film Coated Tablet 10 mg contains 10 mg of Hydroxyzine hydrochloride
Voxyzine Hydroxyzine HCl Film Coated Tablet 25 mg contains 25 mg of Hydroxyzine hydrochloride

Excipients with known effect
Lactose
Sodium as Croscarmellose Sodium

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Voxyzine Hydroxyzine HCl Film Coated Tablet 10 mg:
A yellow color film coated round tablet.



Voxyzine Hydroxyzine HCl Film Coated Tablet 25 mg:
A white color film coated oblong tablet, one side with a score.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Minor manifestations of anxiety in adults,
- Premedication for general anesthesia,
- Symptomatic treatment of pruritus,
- In children over 6 years of age, second-line treatment of sleep-onset insomnia related to a state of hyper-arousal (increased vigilance linked to anxious manifestations at bedtime), after failure of behavioral measures alone.

4.2 Dosage and method of administration

The tablet is not a suitable form for children under 6 years of age (risk of choking).
Oral Route

Dosage
Voxyzine Hydroxyzine HCl Film Coated Tablet should be taken at the lowest effective dose and for the shortest possible duration of treatment.

Adults
- Minor manifestations of anxiety: 50 mg/day in 3 separate doses of 12.5 mg - 12.5 mg - 25 mg. For more severe cases, doses up to 100 mg/day may be used.
- Symptomatic treatment of pruritus: An initial dose of 25 mg before bedtime, followed if necessary by doses of up to 25 mg, 3 to 4 times daily.
- Premedication for general anesthesia: 100 mg in adults.

In adults, the maximum daily dose is 100 mg.

Elderly subject
It is recommended to initiate treatment with half the recommended dose due to the prolonged effect. The lowest possible dose should be chosen when treating elderly patients.

The maximum daily dose is 50 mg.

Liver failure
It is recommended to reduce the dosage by half.

Kidney failure
No dose adjustment is necessary in patients with slightly impaired renal function (glomerular filtration rate (GFR) 60 - <90 mL/min).

The prescriber should adjust the dose according to the individual patient's response for patients with moderately reduced renal function (GFR 30 - 60 mL/min) because the available data are limited to recommend a specific dose adjustment.

A 50% dose adjustment is recommended in patients with severely impaired renal function (GFR < 30 mL/min not requiring dialysis).

Hydroxyzine is contraindicated in patients with end-stage renal disease (ESRD) (GFR <15 mL/min requiring dialysis).

Pediatric population
- In sleep onset insomnia in children over 6 years of age: the suggested dosage as a guide is 1 mg/kg/day, and the treatment will be of short duration (2 weeks maximum).
- For the symptomatic treatment of pruritus:
  In children aged 6 years and over: 1 mg/kg/day up to 2 mg/kg/day in divided doses.
- In other indications in children aged 6 to 15 years: the recommended dose is 1 mg/kg/day.

For children up to 40 kg, the maximum daily dose is 2 mg/kg/day.
For children over 40 kg, the maximum daily dose is 100 mg.

Method of Administration
Voxyzine Hydroxyzine HCl Film Coated Tablet is for oral use.

4.3 Contraindications
- Patients who have shown previous hypersensitivity to hydroxyzine hydrochloride, cetirizine, other piperazine derivatives, aminophylline or ethylenediamine, or any of the excipients of this medicinal product.
- 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.
- Asthmatics who have previously experienced a serious anti-histamine-induced adverse bronchopulmonary effect.
- Porphyria.
- Pregnancy and breast-feeding.
- Contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.4 Special warnings and precautions for use
Prolongation of the QT interval
Hydroxyzine is associated with prolongation of the QT interval on the electrocardiogram. During post-marketing surveillance, cases of QT prolongation and torsade de pointes have been reported in patients taking hydroxyzine. Most of these patients had other risk factors, electrolyte abnormalities and concomitant treatment which may have contributed. Hydroxyzine should be used at the lowest effective dose and for the shortest possible treatment duration. Hydroxyzine treatment should be discontinued if signs or symptoms that may be associated with cardiac arrhythmia occur, and patients should seek medical attention immediately. Patients should be informed of the need to promptly report any cardiac symptoms.

Elderly subjects
Hydroxyzine is not recommended in elderly patients due to the decreased elimination of hydroxyzine in this population compared to the adult population and the higher risk of adverse effects (e.g. anticholinergic effects). It is recommended to initiate treatment with half the recommended dose due to the prolonged effect. Patients should be advised not to drink alcoholic beverages during treatment.

Precautions for use
The administration of hydroxyzine is not recommended in patients with cognitive disorders or confusion syndrome due to the risk of worsening associated with the pharmacodynamic properties of the product.
Due to its potential anticholinergic effects, hydroxyzine should be used with caution in patients with glaucoma, urinary retention, decreased gastrointestinal motility, severe myasthenia gravis, or dementia.
Treatment should be discontinued at least 5 days (7 days in the elderly) before performing an allergy test or methacholine bronchial provocation test to avoid any effect on the test result.

This medicine should be used with caution:
• in young children, who are more particularly sensitive to effects on the central nervous system (in particular convulsions),
• in the event of severe hepatic and/or renal insufficiency, due to the risk of accumulation.

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

Sodium
Voxyzine Hydroxyzine HCl Film Coated Tablet contains less than 1 mmol sodium (23 mg) per film coated 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 gastrointestinal 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.

Associations requiring precaution of use
Caution with bradycardia and hypokalaemia-inducing drugs. Hydroxyzine is metabolized by alcohol dehydrogenase and CYP3A4/5 and an increase in hydroxyzine blood concentrations may be expected when hydroxyzine is co-administered with drugs known to be potent inhibitors of these enzymes.

Hydroxyzine may also have the following interactions:

Methacholine test	Treatment should be stopped for 96 hours prior to a methacholine test, to avoid effects on the test results.
Skin testing for allergy	Treatment should be stopped at least one week before skin testing for allergy to avoid effects on the test results.
CNS depressants	Patients should be warned that hydroxyzine may enhance their response to alcohol, barbiturates, benzodiazepines, hypnotics, opioids, anxiolytics, antipsychotics, antidepressants, antiemetics, antiepileptics, other antihistamines, skeletal muscle relaxants, sedatives, anaesthetics and other CNS depressants.
Antimuscarinics	Antimuscarinic side effects (both peripheral and central) may be increased if hydroxyzine is given with antimuscarinics such as atropine and some antidepressants (both tricyclics and MAOIs).
Adrenaline	Hydroxyzine has been shown to inhibit and reverse the vasopressor effect of adrenaline.
Anticholinergic agents	Additive anticholinergic effects may occur if hydroxyzine is administered concomitantly with other anticholinergic agents.
Anticholinesterase drugs	Hydroxyzine may antagonise the effects of anticholinesterase drugs.
Betahistine	Hydroxyzine may antagonise the effects of betahistine.
Cimetidine	Cimetidine, 600 mg twice a day, has been shown to increase the serum concentrations of hydroxyzine and to decrease peak concentrations of the metabolite cetirizine.
CYP2D6 & cytochrome P450	Hydroxyzine is an inhibitor of CYP2D6 and may cause drug-drug interactions with CYP2D6 substrates. Cetirizine does not interact with other drug substances via cytochrome P450.
Drugs which have effects on the brain	Drugs which have effects on the brain will interact with antihistamines.
Drugs that affect the hepatic microsomal enzyme system	Metabolism may be reduced in patients concomitantly receiving drugs that affect the hepatic microsomal enzyme system. Decreased metabolism may result in accumulation of potentially toxic concentrations of unchanged antihistamine.
Ototoxic drugs	It has been suggested that some sedating antihistamines could mask the warning signs of damage caused by ototoxic drugs such as aminoglycoside antibiotics.
Porter-Silber reaction or the Glenn-Nelson method	Hydroxyzine has been reported to cause falsely elevated urinary concentrations of 17-hydroxycorticosteroids when the Porter-Silber reaction or the Glenn-Nelson method is used.

4.6 Fertility, pregnancy and lactation

Pregnancy

Hydroxyzine tablets should not be used during pregnancy. Clinical data in humans are inadequate to establish safety in early pregnancy. The use of sedating antihistamines in the latter part of the third trimester may cause adverse effects in neonates such as irritability, paradoxical excitability, and tremor. Animal studies have shown reproductive toxicity. Foetal abnormalities have been reported when hydroxyzine was administered, at doses substantially above the human therapeutic dose, to the pregnant mouse, rat and rabbit. Hydroxyzine crosses the placental barrier which may lead to higher foetal than maternal concentrations. The following events were observed in a neonate whose mother received high dose (600 mg per day) hydroxyzine during pregnancy; hypotonia, movement disorders including extrapyramidal disorders, clonic movements, tachypnea and poor feeding.

Lactation

It is expected that hydroxyzine may be excreted into breast milk. The effects on the nursing infant are unknown. Hydroxyzine should not be given to nursing mothers.

4.7 Effects on ability to drive and use machines

Patients should be warned that hydroxyzine may impair their ability to perform activities requiring mental alertness or physical co-ordination such as operating machinery or driving a vehicle. Concomitant use of hydroxyzine with alcohol or other CNS depressants should be avoided as this may aggravate these effects.

4.8 Undesirable effects

The most common adverse 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 headache, psychomotor impairment and antimuscarinic effects.

Undesirable effects are listed by MedDRA System Organ Classes.

Assessment of undesirable effects is based on the following frequency groupings:
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

System Organ Class	Undesirable Effect	Frequency
Blood and lymphatic system disorders	blood disorders, including agranulocytosis, leukopenia, haemolytic anaemia, and thrombocytopenia	Not known
Immune system disorders	hypersensitivity reactions, anaphylaxis, angioedema	Not known
Metabolic and nutritional disorders	porphyria, anorexia	Not known
Psychiatric disorders	agitation, confusion, disorientation, hallucinations, sleep disturbances, depression, increased anxiety, nightmares	Not known
Nervous system disorders	dyskinesia[4], insomnia, sedation, drowsiness, dizziness, weakness, headache, tremor[1], convulsions[2], psychomotor impairment, paraesthesia, extrapyramidal effects, seizure, coma, somnolence. Disturbance in attention, involuntary motor activity[3], ataxia, slurred speech, bitter taste in mouth, faintness	Not known
Eye disorders	accommodation disorder, blurred vision	Not known
Ear and labyrinth disorders	tinnitus, labyrinthitis, vertigo	Not known
Cardiac disorders	ventricular arrhythmias (e.g. Torsade de Pointes), QT interval prolongation, tachycardia, palpitation	Not known
Vascular disorders	hypotension, flushing	Not known
Respiratory, thoracic and mediastinal disorders	respiratory tract secretions, wheezing, nasal stuffiness, dryness of throat	Not known
Gastrointestinal disorders	constipation, dryness of the mouth, nausea, vomiting, increased gastric reflux, diarrhoea, epigastric pain, increased GI peristalsis	Not known
Hepatobiliary disorders	liver dysfunction	Not known
Skin and subcutaneous tissue disorders	dermatitis, fixed drug eruption, pruritus, erythema, popular rash, sweating increased, urticaria, hair loss, eczema, acute generalised exanthematous pustulosis (AGEP), toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme	Not known
Musculoskeletal and connective tissue disorders	myalgia	Not known
Renal and urinary disorders	urinary retention, dysuriaa	Not known
Reproductive system and breast disorders	priapism, impotence, early menses	Not known
General disorders and administration site conditions	fatigue, malaise, lassitude, pyrexia, dryness of respiratory mucosae, asthenia, tightness of chest, irritability, chills	Not known
Investigations	liver function tests abnormal, weight increased	Not known

Footnotes
[1, 2, 3] reported usually with doses considerably higher than those recommended. Continuous therapy with over 1 g/day has been employed in some patients without these effects having been encountered.
[4] dyskinesia may follow termination of prolonged antihistamine therapy.
Children and the elderly are more susceptible to side-effects.

4.9 Overdose
Overdosage with sedating antihistamines is associated with antimuscarinic, extrapyramidal, and CNS effects. If CNS stimulation predominates over CNS depression, ataxia, excitement, seizures, tremors, psychoses, hallucinations, convulsions, and hyperpyrexia can occur. Coma and cardiorespiratory collapse may follow. CNS stimulation is more likely in children and elderly. In adults, CNS depression is more common with drowsiness, postictal depression, coma, and convulsions, progressing to respiratory failure and cardiovascular collapse. In children and adults, cerebral oedema and upper nephron nephrosis, a deepening coma, tachycardia, QRS widening, heart block, cardiorespiratory collapse/arrest, cardiogenic shock, and death may occur.

Common features include excessive sedation, nausea, vomiting, flushing, dilated pupils, dry mouth and tongue, hot dry skin, fever, sinus tachycardia, hypertension, ataxia, nystagmus, delirium, agitation, psychosis and visual hallucinations. Uncommon systemic features include myoclonic jerking, muscle rigidity, coma, convulsions, cardiac conduction abnormalities, QT prolongation and arrhythmias, cardiovascular collapse, paralytic ileus, urinary retention, hyperkalaemia, metabolic acidosis and rhabdomyolysis.

Peak concentrations occur approximately two hours post ingestion, and elimination half-life has been reported approximately 14 hours and 20 hours post ingestion.

There is no specific antidote. It is doubtful whether haemodialysis or peritoneal dialysis has any value in the treatment of overdosage with hydroxyzine. However, if other agents such as barbiturates have been ingested concomitantly, dialysis may be indicated.

Consider activated charcoal only if the patient presents within 1 hour of ingestion of a potentially toxic amount. Gastric lavage is rarely required; for substances that cannot be removed effectively by other means, it should be considered only if a life-threatening amount has been ingested within the previous hour. It should be carried out only if the airway can be protected adequately. Induction of emesis is not recommended.

General supportive care, including frequent monitoring of the vital signs and close observation of the patient is indicated. Clear airways should be maintained, and there should be adequate ventilation. Assisted ventilation is indicated if hypercapnia is present. Observation for 6 hours after ingestion, without any other specific treatment, will be sufficient for the majority of patients. Monitor BP, pulse and body temperature. In symptomatic patients measure U&Es and creatine kinase. Perform a 12-lead ECG and monitor cardiac rhythm. Patients who have been unconscious may be hypothermic.

Hypotension, though unlikely, may be controlled with intravenous fluids. In adults, if severe hypotension persists, determine the cause, and consider treatment with the following; if hypotension is mainly due to decreased systemic vascular resistance, drugs such as noradrenaline or high dose dopamine may be beneficial, if hypotension is due to reduced cardiac output dobutamine, or in severe cases adrenaline may be beneficial. However it should be noted that hydroxyzine has been shown to inhibit and reverse the vasopressor effect of adrenaline.

Analeptic agents should not be used since they may cause seizures.

As in the management of overdosage with any drug, it should be borne in mind that multiple agents may have been taken.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

General Properties

Pharmacotherapeutic group: Anxiolytics. ATC code: N05B B01

Hydroxyzine is unrelated chemically to benzodiazepines, phenothiazines, reserpine and meprobamate.

Mechanism of action

Hydroxyzine is a first generation antihistamine, a piperazine derivative, with antimuscarinic and sedative properties. Antihistamines act as competitive antagonists of histamine at H_1 histamine receptors, thus inhibiting H_1 receptor-mediated reactions, such as vasodilation, flare and itch reactions and sneezing. First-generation H_1 antagonists easily cross the blood-brain barrier, consequently producing well-documented sedative and anticholinergic effects. First-generation antihistamines also have affinity for 5-HT receptors, alpha adrenoreceptors, and muscarinic receptors. They also reduce cyclic GMP concentrations, increase atrioventricular nodal conduction, and inhibit activation of airway vagal afferent nerves.

Pharmacodynamic effects

Hydroxyzine has CNS depressant, anticholinergic, antispasmodic, and local anaesthetic activity, in addition to antihistaminic effects. The drug also has sedative, antiemetic and primary skeletal muscle relaxant activity. An onset of sedative action of hydroxyzine is usually noted within 15 to 30 minutes after oral administration. Sedative effects persist for 4-6 hours following administration of a single dose. Hydroxyzine suppresses the inflammatory response (wheal and flare reaction) and pruritus for up to 4 days after intradermal skin tests with allergens and histamine. The therapeutic range for plasma hydroxyzine concentrations and the relationship of plasma concentration to clinical response or toxicity have not been established. Hydroxyzine does not appear to increase gastric secretions or acidity, and usually has mild antisecretory effects. It induces a calming effect in anxious tense adults. It is not a cortical depressant, but its action may be due to a suppression of activity in certain key regions of the subcortical area of the central nervous system.

Clinical efficacy and safety

Hydroxyzine has been shown clinically to be a rapid-acting anxiolytic with a wide margin of safety.

Antihistamine effects have been demonstrated experimentally and confirmed clinically; it is highly effective in alleviating pruritus.

Paediatric population
The pharmacokinetics and antipruritic effects of hydroxyzine 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 drug are low (only 10% of the maximum levels achieved). In children, the biologic effects of hydroxyzine appear to be much more prolonged than would be predicted from the half-life values.

5.2 Pharmacokinetic properties
Absorption
Hydroxyzine is rapidly absorbed from the gastrointestinal tract. After a single oral dose of hydroxyzine, 0.7 mg/kg (mean dose 39.0 +/- 5.4 mg) a mean maximum serum hydroxyzine concentration of 72.5 +/- 11.1 ng/ml has been shown to occur at a mean time of 2.1 +/- 0.4 hours.
Distribution
Distribution of hydroxyzine into human body tissues and fluids has not been fully characterised. Following administration of hydroxyzine to animals, the drug is widely distributed into most body tissues and fluids with highest concentrations in the liver, lungs, spleen, kidneys, and adipose tissue. The drug is also distributed into bile in animals. Hydroxyzine crosses the placental barrier which may lead to higher foetal than maternal concentrations. Serum hydroxyzine concentrations do not necessarily reflect hydroxyzine tissue binding or distribution to skin receptor sites. Suppression of wheals, flares, and associated pruritis has been shown to persist even when serum hydroxyzine concentrations are low. First-generation H_1 antagonists easily cross the blood-brain barrier. In a study group of healthy adults, the mean apparent volume of distribution has been found to be 16.0 +/- 3.0 L/kg.

Biotransformation
Hydroxyzine is metabolised in the liver. Metabolites include cetirizine, which has antihistaminic activity. Cetirizine is formed from hydroxyzine via an oxidative biotransformation step.

Elimination
An elimination half-life of 20.0 +/- 4.1 hours and of 14.0 hours has been reported for hydroxyzine. Total body clearance in adults is generally in the range of 5 to 12 ml/min/kg. Hydroxyzine is eliminated by hepatic metabolism in humans. Cetirizine is mainly renally excreted.

Special Populations
Elderly
The pharmacokinetics of hydroxyzine were studied in nine healthy elderly (mean age 69.5 +/- 3.7 years) subjects who ingested a single dose of hydroxyzine, 0.7 mg/kg (mean dose 49.0 +/- 6.7 mg). The mean serum elimination half-life value of hydroxyzine in this elderly group was 29.3 +/-10.1 hours (range 20.2 to 53.3 hours), which was significantly longer than that reported in younger subjects. The mean apparent volume of distribution of hydroxyzine in this elderly group was 22.5 +/- 6.3 L/kg (range 13.4 to 30.7 L/kg), which was significantly larger than that reported to be found in young adults. Hydroxyzine has a long mean serum elimination half-life value, a large volume of distribution and a prolonged pharmacodynamic effect (suppressive effect on wheal and flare response to histamine) in the elderly. In the elderly a number of age-related biological and physiological changes may have an effect on the pharmacology of hydroxyzine and its metabolite, cetirizine. These changes may impact upon the pharmacologic functions of absorption, distribution, metabolism, excretion, and receptor sensitivity. Dosage reduction may be appropriate in elderly patients.

Paediatric patients
The pharmacokinetics and antipruritic effects of hydroxyzine hydrochloride was studied in 12 children aged 1 to 14 years (mean age 6.1 +/- 4.6 years) with severe atopic dermatitis. The children were given a single orally administered dose of 0.7 mg/kg hydroxyzine. The mean peak serum concentration of 47.4 +/- 17.3 ng/ml occurred at a mean time of 2.0 +/- 0.9 hours. Terminal elimination half-life was shorter in children than in adults, at a mean of 7.1+/- 2.3 hours. This resulted from a larger clearance rate in children of 32.08 +/- 11.05 ml/min/kg. The elimination half-life values increased with increasing age. Half-life values were approximately 4 hours in the 1 year old patients and 11 hours in the 14 year old patient.
Dosage should be adjusted in the paediatric population.

Hepatic Impairment
The pharmacokinetics and pharmacodynamics of hydroxyzine were studied in eight patients (mean age 53.4 +/- SD11.2 years) with primary biliary cirrhosis, given a single dose of 0.7 mg/kg (mean dose 43.9 +/- 6.6 mg) hydroxyzine. All patients had abnormal liver biochemistry tests, all had biopsies compatible with primary biliary cirrhosis, and seven of eight had positive tests for antimitochondrial antibodies. Hydroxyzine elimination was found to be impaired in patients with primary biliary cirrhosis. Mean peak hydroxyzine levels occurring at 2.3 +/- 0.7 hours were found to be 116.5 +/- 60.6 ng/ml, which was significantly higher than in other patient groups studied previously. Mean serum elimination half life of hydroxyzine was 36.6 +/- 13.1 hours, which was significantly longer than in patients with normal hepatic function studied previously. Dosage should be adjusted in patients with hepatic impairment.

Renal Impairment
The pharmacokinetics of hydroxyzine and of its active metabolite cetirizine were

studied in patients with reduced kidney function. Eight healthy volunteers and eight patients with renal insufficiency received a single peroral dose of 50 mg hydroxyzine. With regards to hydroxyzine, results showed moderate elevation of the average terminal half-life in the patients group ($t_{1/2}$ 14 vs. 23 h). The areas under the concentration-time curves (AUC) were 996 ng/h/ml-1 in the healthy volunteers group and 1621 ng/h/ml^{-1} in the patients group. For cetirizine, AUC measured 6036 ng/h/ml^{-1} in the healthy volunteers group and 31635 ng/h/ml^{-1} in the patients group. The study concluded that the reduced renal clearance of cetirizine may be of clinical importance in patients with renal failure. Dosage should be adjusted in patients with renal impairment.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal Silicon Dioxide
Croscarmellose Sodium
Dimethylpolysiloxane
Hydroxypropyl methylcellulose
Lactose
Magnesium Stearate
Microcrystalline Cellulose
Polyethylene Glycol

Voxyzine Hydroxyzine HCl Film Coated Tablet 10 mg also contains:
Iron Oxide Yellow

6.2 Shelf life

Voxyzine Hydroxyzine HCl Film Coated Tablet 10 mg: 2 years
Voxyzine Hydroxyzine HCl Film Coated Tablet 25 mg: 30 months

6.3 Special precautions for storage

Store at temperature below 30°C.

6.4 Nature and contents of container

Voxyzine Hydroxyzine HCl Film Coated Tablet 10 mg
blister pack: 10's x 10

Voxyzine Hydroxyzine HCl Film Coated Tablet 25 mg
blister pack: 10's x 10

6.5 Special precautions for disposal

Not applicable.

7 MANUFACTURER AND PRODUCT REGISTRATION HOLDER

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8 DATE OF REVISION OF THE TEXT

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