AVTORIYA

For the use of a Registered Medical Practitioner, a Hospital or a Laboratory only.

Trade name: Avtoriya.
International Nonproprietary Name: Hydroxyzine.
Dosage form: film-coated tablets.
Composition: each film-coated tablet contains:
Hydroxyzine Hydrochloride USP 25 mg.
Pharmacotherapeutic group: Tranquilizer (anxiolytic).
ATC Classification: N05BB01.
Pharmacologic property:
Pharmacodynamics:
Hydroxyzine is a first generation antihistamine, a piperazine derivative, with antimuscarinic and sedative properties.
Antihistamines act as competitive antagonists of histamine at H1 histamine receptors, thus inhibiting H1 receptor-mediated reactions, such as vasodilation, flare and itch reactions and sneezing.
First-generation H1 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.
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.
Pharmacokinetics:
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.
Indications:
- to assist in the management of anxiety in adults;
- for the management of pruritus associated with acute and chronic urticaria, including cholinergic and physical types, and atopic and contact dermatitis in adults and children.

Contra-indications:
- patients who have shown previous hypersensitivity to hydroxyzine hydrochloride, cetirizine, other piperazine derivatives, aminophylline or ethylenediamine, or any of the excipients of Avtoriya;
- asthmatics who have previously experienced a serious anti-histamine-induced adverse bronchopulmonary effect;
- porphyria;
- pregnancy and lactation.

Dosage and directions for use:
Method of administration: oral.
For symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in organic disease states in which anxiety is manifested: in adults, 50–100 mg q.i.d.; children under 6 years, 50 mg daily in divided doses and over 6 years, 50–100 mg daily in divided doses.
For use in the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatoses, and in histamine-mediated pruritus: in adults, 25 mg t.i.d. or q.i.d.; children under 6 years, 50 mg daily in divided doses and over 6 years, 50–100 mg daily in divided doses.
As a sedative when used as a premedication and following general anesthesia: 50–100 mg in adults, and 0.6 mg/kg in children.
As with all medications, the dosage should be adjusted according to the patient's response to therapy.
Hepatic impairment the total daily dose should be reduced by 33%. Use in patients with severe liver disease should be avoided.
Renal impairment for patients with moderate or severe renal impairment, it is recommended that the total daily dosage should be reduced by 50%.
Side-effects:
Nervous system: insomnia, sedation, drowsiness, dizziness, weakness, headache, psychomotor impairment, seizure, somnolence, disturbance in attention, ataxia, faintness.
Eye disorders: accommodation disorder, blurred vision.
Renal and urinary: urinary retention, dysuria.
Cardiac disorders: tachycardia, palpitation.
Gastrointestinal: constipation, dryness of the mouth, nausea, vomiting, increased gastric reflux, diarrhoea, epigastric pain, increased GI peristalsis.
Other: bronchospasm, allergic reactions, increased sweating.
Overdose:
Symptoms: increased anticholinergic effects, depression or paradoxical CNS stimulation, nausea, vomiting, involuntary motor activity, hallucinations, impaired consciousness, arrhythmia, hypotension, rarely - tremors, convulsions, disorientation that occur when large overdose.
Treatment: If vomiting has not occurred spontaneously, it should be induced. Immediate gastric lavage is also recommended. General supportive care, including frequent monitoring of the vital signs and close observation of the patient, is indicated. Hypotension, though unlikely, may be controlled with intravenous fluids and levarterenol or metaraminol. Do not use epinephrine as Avtoriya counteracts its pressor action.
There is no specific antidote. It is doubtful that hemodialysis would be of any value in the treatment of overdosage with hydroxyzine.
Drug interactive:
Patients should be warned that Avtoriya may enhance their response to alcohol, barbiturates, benzodiazepines, hypnotics, opioids, anxiolytics, antipsychotics, antidepressents, antiemetics, antiepileptics, other antihistamines, skeletal muscle relaxants, sedatives, anaesthetics and other CNS depressants.
Hydroxyzine may antagonise the effects of anticholinesterase drugs. Hydroxyzine may antagonise the effects of betahistine. Cimetidine, 600mg twice a day, has been shown to increase the serum concentrations of hydroxyzine and to decrease peak concentrations of the metabolite cetirizine
CYP2D6 and 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.
Cautions:
If necessary of allergy tests, taking hydroxyzine should be discontinued 5 days prior to the study.
Effects on ability to drive and use machines:
Patients should be warned that Avtoriya 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.
Presentation:
Box of 2 blisters of 10 film coated tablets with instruction for use.
Storage:
Keep in dry place, protected from light at a temperature below 25°C. Keep out of reach of children.
Shelf life:
Labeled. The preparation should not be used after the expiry date.
Distribution Condition:
Prescribed medicine.

SPEY

Manufactured for:
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