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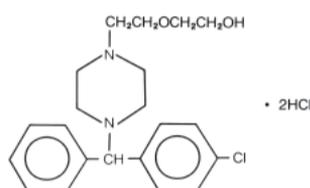
**HYDROXYZINE
HYDROCHLORIDE
INJECTION, USP**

Rx only

FOR INTRAMUSCULAR USE ONLY
DESCRIPTION:

Hydroxyzine Hydrochloride Injection, USP is a sterile, aqueous solution intended for intramuscular administration only.

Hydroxyzine hydrochloride is chemically designated as 2-[2-[4-(p-Chloro-α-phenylbenzyl)-1-piperaziny]ethoxy]ethanol dihydrochloride and has the following structural formula:


 $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$
M.W. 447.83

Hydroxyzine hydrochloride occurs as a white, odorless powder which is very soluble in water.

Each mL contains: 25 or 50 mg hydroxyzine hydrochloride; 0.9% benzyl alcohol; Water for Injection q.s. Hydrochloric acid and/or sodium hydroxide may have been added for pH adjustment (3.5 to 6.0).

CLINICAL PHARMACOLOGY:

Hydroxyzine hydrochloride is unrelated chemically to the phenothiazines, reserpine, meprobamate or the benzodiazepines. Hydroxyzine 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 (CNS).

Primary skeletal muscle relaxation has been demonstrated experimentally. Bronchodilator activity and antihistaminic and analgesic effects have been demonstrated experimentally and confirmed clinically. An antiemetic effect, both by the apomorphine test and the veriloid test, has been demonstrated.

Pharmacological and clinical studies indicate that hydroxyzine in therapeutic dosage does not increase gastric secretion or acidity and in most cases has mild antisecretory activity.

INDICATIONS AND USAGE:

For symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in organic disease states in which anxiety is manifested.

Useful in the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatoses and in histamine-mediated pruritus.

As a sedative when used as a premedication and following general anesthesia. Hydroxyzine is not known to interfere with the action of digitalis in any way and it may be used concurrently with this agent.

The effectiveness of hydroxyzine as an anti-anxiety agent for long term use, that is more than four months, has not been assessed by systematic clinical studies. The physician should reassess periodically the usefulness of the drug for the individual patient.

CONTRAINDICATIONS:

Hydroxyzine, when administered to the pregnant mouse, rat and rabbit, induced fetal abnormalities in the rat and mouse at doses substantially above the human therapeutic range. Clinical data in human beings are inadequate to establish safety in early pregnancy. Until such data are available, hydroxyzine is contraindicated in early pregnancy.

Hydroxyzine hydrochloride is contraindicated for patients who have shown a previous hypersensitivity to it.

Hydroxyzine hydrochloride injection is intended only for intramuscular administration and should not, under any circumstances, be injected subcutaneously, intra-arterially or intravenously.

WARNINGS:

Tissue damage: Intramuscular hydroxyzine hydrochloride may result in severe injection site reactions (including extensive tissue damage, necrosis and gangrene) requiring surgical intervention (including debridement, skin grafting and amputation).

PRECAUTIONS:

THE POTENTIATING ACTION OF HYDROXYZINE MUST BE CONSIDERED WHEN THE DRUG IS USED IN CONJUNCTION WITH CENTRAL NERVOUS SYSTEM DEPRESSANTS SUCH AS NARCOTICS, BARBITURATES AND ALCOHOL. Rarely, cardiac arrests and death have been reported in association with the combined use of hydroxyzine hydrochloride intramuscularly and other CNS depressants. Therefore, when CNS depressants are administered concomitantly with hydroxyzine their dosage should be reduced up to 50%. The efficacy of hydroxyzine as adjunctive pre- and postoperative sedative medication has also been well established, especially with regards to its ability to allay anxiety, control emesis and reduce the amount of narcotic required.

HYDROXYZINE MAY POTENTIATE NARCOTICS AND BARBITURATES, so their use in preanesthetic adjunctive therapy should be modified on an individual basis. Atropine and other belladonna alkaloids are not affected by the drug.

When hydroxyzine is used preoperatively, narcotic requirements may be reduced as much as 50%. Thus, when 50 mg of hydroxyzine hydrochloride is employed, meperidine dosage may be reduced from 100 mg to 50 mg. The administration of meperidine may result in severe hypotension in the postoperative patient or any individual whose ability to maintain blood pressure has been compromised by a depleted blood volume. Meperidine should be used with great caution and in reduced dosage in patients who are receiving other pre- and/or postoperative medications and in whom there is a risk of respiratory depression, hypotension and profound sedation or coma occurring. Before using any medications concomitant with hydroxyzine, the manufacturer's prescribing information should be read carefully.

Since drowsiness may occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery while taking hydroxyzine. Patients should also be advised against the simultaneous use of other CNS depressant drugs and cautioned that the effects of alcohol may be increased.

Inject well within the body of a relatively large muscle. Inadvertent subcutaneous injection may result in significant tissue damage.

Adults

The preferred site is the upper outer quadrant of the buttock (i.e., the gluteus maximus) or the mid-lateral thigh.

Children

It is recommended that intramuscular injections be given preferably in the mid-lateral muscles of the thigh. In infants and small children, the periphery of the upper outer quadrant of the gluteal region should be used only when necessary, such as in burn patients, in order to minimize the possibility of damage to the sciatic nerve.

The deltoid area should be used only if well developed such as in certain adults and older children, and then only with caution to avoid radial nerve injury. Intramuscular injections should not be made into the lower and mid-third of the upper arm. As with all intramuscular injections, aspiration is necessary to help avoid inadvertent injection into a blood vessel.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Since many drugs are so excreted, hydroxyzine should not be given to nursing mothers.

ADVERSE REACTIONS:

Therapeutic doses of hydroxyzine seldom produce impairment of mental alertness. However, drowsiness may occur; if so, it is usually transitory and may disappear in a few days of continued therapy or upon reduction of the dose. Dryness of the mouth may be encountered at higher doses. Extensive clinical use has substantiated the absence of toxic effects on the liver or bone marrow when administered in the recommended doses for over four years of uninterrupted therapy. The absence of adverse effects has been further demonstrated in experimental studies in which excessively high doses were administered.

Involuntary motor activity, including rare instances of tremor and convulsions, has been 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.

OVERDOSAGE:

The most common manifestation of hydroxyzine overdosage is hypersedation.

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 norepinephrine or metaraminol. Do not use epinephrine as hydroxyzine 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. However, if other agents such as barbiturates have been ingested concomitantly, hemodialysis may be indicated. There is no practical method to quantitate hydroxyzine in body fluids or tissue after its ingestion or administration.

DOSAGE AND ADMINISTRATION:

For symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in organic disease states in which anxiety is manifested: Adults, 50 to 100 mg q.i.d.

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: Adults, 25 mg t.i.d. or q.i.d.

As a sedative when used as a premedication and following general anesthesia: 50 to 100 mg for adults, and 0.6 mg/kg of body weight in children.

When treatment is initiated by the intramuscular route of administration, subsequent doses may be administered orally.

As with all potent medication, the dosage should be adjusted according to the patient's response to therapy.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED:

Hydroxyzine Hydrochloride Injection, USP is available in the following concentrations:

Product No.	NDC No.	Description
2101	63323-021-01	25 mg per mL, 1 mL fill in a 2 mL flip-top vial, in packages of 25.
5101	63323-051-01	50 mg per mL, 1 mL fill in a 2 mL flip-top vial, in packages of 25.
5102	63323-051-02	100 mg per 2 mL (50 mg per mL), 2 mL fill, in a 2 mL flip-top vial, in packages of 25.

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

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/s/

ROBERT L WEST

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Deputy Director, Office of Generic Drugs, for
Kathleen Uhl, M.D.