When given concurrently the following drugs may interact with thiazide diuretics.

**Drug Interactions**

Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be done at appropriate intervals.

**Laboratory Tests**

Increases in cholesterol and triglyceride levels may be associated with thiazide diuretic therapy.

**Thiazides should be discontinued before carrying out tests for parathyroid function.** Marked hypercalcemia may be evidence of hidden hyperparathyroidism. Thiazides should be discontinued before carrying out tests of calcium metabolism. The serum calcium concentration should be determined 48 to 72 hours after the drug has been discontinued. If marked hypercalcemia is present, the patient should be given intravenous fluids and, if necessary, parenteral calcium-free milk or a milk substitute containing phosphate. The patient should be observed for evidence of improvement.

Thiazides have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia. If progressive renal impairment becomes evident, consider withholding or discontinuing diuretic therapy.

The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient.

Diabetes mellitus may become manifest during thiazide therapy.

**Restlessness, confusion, seizures, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as**

**Warning signs or symptoms of fluid and electrolyte imbalance, irrespective of cause, include dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, confusion, seizures, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting.**

**General**

All patients receiving diuretic therapy should be observed for evidence of fluid or electrolyte imbalance: namely, hypovolemia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Use of diuretics to lower intravascular volume in this instance is illogical and unnecessary. During normal pregnancy there is a hypercalcemia which is not harmful to the fetus or the mother in the absence of cardiovascular disease. However, it may be associated with edema, rarely generalized edema. If such edema causes discomfort, increased recumbency will often provide relief. Rarely this edema may cause extreme discomfort which is not relieved by rest. In these instances, a short course of diuretic therapy may provide relief and be appropriate.

**Contraindications**

Hypersensitivity to any component of this product or to other sulfonamide-derived drugs.

**Warnings**

Intravenous use in infants and children has been limited and is not generally recommended. Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma. Thiazides may add to or potentiate the action of other antihypertensive drugs.

Diuretics may lower blood pressure sufficiently to overcome the pressor response to injection of pressor amines. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient.

**Precautions**

**Drug Interactions**

Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be done at appropriate intervals. Alcohol, barbiturates, or narcotics - potentiation of orthostatic hypotension may occur.

**Contraindications**

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Diuretics may lower blood pressure sufficiently to overcome the pressor response to injection of pressor amines. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient.

**Precautions**

**Drug Interactions**

Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be done at appropriate intervals. Alcohol, barbiturates, or narcotics - potentiation of orthostatic hypotension may occur.
**Antidotal drugs - (oral agents and insulin) - dosage adjustment of the antidotal drug may be required.**

Other antihypertensive drugs - additive effect or potentiation.

Curarecontroagents, ACH - intensified electrolyte depletion, particularly hypokalemia.

Pressure amine (e.g., norepinephrine) - possible decreased response to pressor amines but not sufficient to preclude their use.

Skeletal muscle relaxants, nondepolarizing (e.g., tubocurarine) - possible increased responsiveness to the muscle relaxant.

Lithium - generally should not be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the package insert for lithium preparations before use of such preparations with chlorothiazide sodium for injection.

**Nonsteroidal Anti-inflammatory Drugs** - in some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium-sparing and thiazide diuretics. Therefore, when chlorothiazide sodium for injection and non-steroidal anti-inflammatory agents are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

**Drug/Laboratory Test Interactions**

Thiazides should be discontinued before carrying out tests for parathyroid function (see PRECAUTIONS, General).

**Canicominogenesis, Mutagenesis, Impairment of Fertility**

Canicominogenesis studies have not been conducted with chlorothiazide.

Chlorothiazide was not mutagenic in vitro in the Ames microbial mutagen test (using a maximum concentration of 5 mg/ml and Salmonella typhimurium strains TA98 and TA100) and was not mutagenic and did not induce nitroreduction in diploid strains of Aspergillus nidulans.

Chlorothiazide had no adverse effects on fertility in female rats at doses up to 60 mg/kg/day and no adverse effects on fertility in male rats at doses up to 40 mg/kg/day. These doses are 1.5 and 1.0 times** the recommended maximum human dose, respectively, when compared on a body weight basis.

**Pregnancy**

Teratogenic Effects - Pregnancy Category C: Although reproduction studies performed with chlorothiazide doses of 50 mg/kg/day in rabbits, 60 mg/kg/day in rats and 500 mg/kg/day in mice revealed no external abnormalities of the fetus or impairment of growth and survival of the fetus due to chlorothiazide, such studies did not include examinations for visceral and skeletal abnormalities. It is not known whether chlorothiazide can cause fetal harm when administered to a pregnant woman; however, thiazides cross the placental barrier and appear in cord blood. Chlorothiazide sodium for injection should be used during pregnancy only if clearly needed (see INDICATIONS AND USAGE).

Nonteratogenic Effects: Chlorothiazide may cause fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

**Nursing Mothers**

Because of the potential for serious adverse reactions in nursing infants from chlorothiazide sodium for injection, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**Pediatric Use**

Safety and effectiveness of chlorothiazide sodium for injection in pediatric patients have not been established.

**Geriatric Use**

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

**Clinical Studies of Chlorothiazide Sodium for Injection**

The intravenous LD50 of chlorothiazide sodium for injection did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. This medication is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see WARNINGS).

**ADVERSE REACTIONS**

The following adverse reactions have been reported and, within each category, are listed in order of decreasing severity.

**Body as a Whole**

Cardiovascular: Hypotension including orthostatic hypotension (may be aggravated by alcohol, barbiturates, narcotics or antihypertensive drugs).

Diaphragm Paralysis, jaundice (intraperitoneal chlorothiazide), jaundice, vomiting, slaladism, cramping, constipation, gastric irritation, nausea, anorexia.

Hematologic: Aplastic anemia, agranulocytosis, leukopenia, hemolytic anemia, thrombocytopenia.

Hypersensitivity: Anaphylactic reactions, necrotizing angitis (vasculitis and cutaneous vasculitis), respiratory distress including pneumonia and pulmonary edema, photosensitivity, fever, urticaria, rash, purpura.

Metabolic: Electrolyte imbalance 임 (see PRECAUTIONS), hyperglycemia, glycuria, hyperuricemia.

Musculoskeletal: Muscle spasm.

Nervous System/Psychiatric: Vertigo, paresthesias, dizziness, headache, restlessness.

Skin: Ekrynema multiforme including Stevens-Johnson syndrome, exfoliative dermatitis including toxic epidermal necrolysis, alopecia.

Special Senses: Transient blurred vision, xanthopphobia.

Renal: Renal failure, renal dysfunction, interstitial nephritis, (see WARNINGS): hematuria (following intravenous use).

Urogenital: Impotence.

Whenever adverse reactions are moderate or severe, thiazide dosage should be reduced or therapy withdrawn.

To report SUSPECTED ADVERSE REACTIONS, contact American Regent, Inc. at 1-800-734-9236 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DOSAGE AND ADMINISTRATION**

Chlorothiazide sodium for injection, USP should be reserved for patients unable to take oral medication or for emergency situations.

Therapy should be individualized according to patient response. Use the smallest dosage necessary to achieve the required response.

**Pharmacokinetics**

The most common signs and symptoms observed are those caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive diuresis. It has also been administered, hygroscopy may accentuate cardiac arrhythmias.

In the event of overdosage, symptomatic and supportive measures should be employed. Correct dehydration, electrolyte imbalance, hepatic coma and hypotension by established procedures. If required, give oxygen or artificial respiration for respiratory impairment.

The degree to which chlorothiazide sodium is removed by hemodialysis has not been established.

The intravenous LD50 of chlorothiazide in the mouse is 1.1 g/kg.

**USE IN CONDITIONS OF IMPAIRED OR ENHANCED RENAL FUNCTION**

The usual adult dosage is 50 mg to 1 g once or twice a day. Many patients with edema respond to intermittent therapy, i.e., administration on alternate days or three to five days each week. With an intermittent schedule, excessive response and the resulting undesirable electrolyte imbalance are less likely to occur.

Therapy should be individualized according to patient response. Use the smallest dosage necessary to achieve the required response.

When medication can be taken orally, therapy with chlorothiazide tablets or oral suspension may be substituted for intravenous therapy, using the same dosage schedule as for the parenteral route.

Chlorothiazide sodium for injection, USP may be given slowly by direct intravenous injection or by intravenous infusion.

**Hepatobiliary**

**Drug/Laboratory Test Interactions**

Nonsteroidal Anti-inflammatory Drugs - (oral agents and insulin) - dosage adjustment of the antidiabetic drug may be required. The use of some diuretics, particularly thiazides, may increase the risk of hypoglycemia in patients with diabetes mellitus and may require an adjustment in insulin dosage. The concomitant use of potassium-sparing diuretics and antihypoglycemic agents may result in a additive effect or potentiation.

Use aseptic technique. Because chlorothiazide sodium for injection, USP contains no preservative, a fresh solution should be prepared immediately prior to each administration, and the unused portion should be discarded.

**Nonteratogenic Effects**

Chlorothiazide was not mutagenic in vitro in the Ames microbial mutagen test (using a maximum concentration of 5 mg/plate and Salmonella typhimurium strains TA98 and TA100) and was not mutagenic and did not induce nitroreduction in diploid strains of Aspergillus nidulans.

In rats and 500 mg/kg/day in mice revealed no external abnormalities of the fetus or impairment of growth and survival of the fetus due to chlorothiazide, such studies did not include examinations for visceral and skeletal abnormalities. It is not known whether chlorothiazide can cause fetal harm when administered to a pregnant woman; however, thiazides cross the placental barrier and appear in cord blood. Chlorothiazide sodium for injection should be used during pregnancy only if clearly needed (see INDICATIONS AND USAGE).

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Use aseptic technique. Because chlorothiazide sodium for injection, USP contains no preservative, a fresh solution should be prepared immediately prior to each administration, and the unused portion should be discarded.

Add 18 ml of Sterile Water for Injection to the vial to form an isotonic solution for intravenous injection. Never add less than 18 ml. When reconstituted with 18 ml of Sterile Water, the final concentration of chlorothiazide sodium for injection, USP is 28 mg/ml. The reconstituted solution is clear and essentially free from visible particles. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to use whenever solution and container permit. The solution is compatible with dextrose or sodium chloride solutions for intravenous infusion. Avoid simultaneous administration of solutions of chlorothiazide with whole blood or its derivatives.

**HOW SUPPLIED**

Chlorothiazide Sodium for Injection, USP is a dry, sterile lyophilized white powder usually in plug form, supplied in vials containing Chlorothiazide Sodium equivalent to 500 mg of Chlorothiazide Sodium.

Individually boxed NDC 0157-1820-01

Storage - store lyophilized powder at 20 to 25°C (68° to 77°F) (See USP Controlled Room Temperature).

For single dose only. Use solution immediately after reconstitution (see DOSAGE AND ADMINISTRATION, Directions for Reconstitution). Discard unused portion of the reconstituted solution.

**、“Calculations based on a human body weight of 50 kg.**