6940

ENDRATE®

EDETATE DISODIUM INJECTION, USP

FOR INTRAVENOUS INFUSION ONLY AFTER DILUTION

Ampul

WARNING
The use of this drug in any particular patient is recommended only when the severity of the clinical condition justifies the aggressive measures associated with this type of therapy.

DESCRIPTION

Endrate (Edetate Disodium Injection, USP) is a sterile, nonpyrogenic, concentrated solution of edetate disodium in water for injection which as a result of a pH adjustment with sodium hydroxide contains varying amounts of disodium and trisodium salts. After dilution, it is administered by intravenous infusion.

Each milliliter (mL) contains edetate disodium, anhydrous 150 mg. May contain sodium hydroxide for pH adjustment. pH is 7.0 (6.5 to 7.5).

Edetate disodium is classified as a clinical chelating agent for emergency lowering of serum calcium in hypercalcemia.

HOW SUPPLIED

Endrate (Edetate Disodium Injection, USP) is supplied in 20 mL (3.0 g) ampuls, List No. 6940.

Store at controlled room temperature 15°C to 30°C (59°F to 86°F).

Caution: Federal (USA) law prohibits dispensing without prescription.

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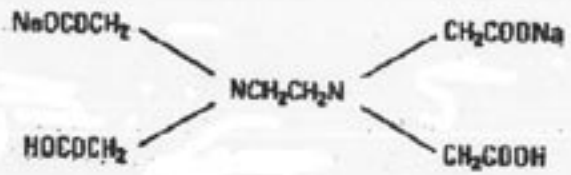
ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

The solution contains no bacteriostat, antimicrobial agent or buffer (except for pH adjustment) and is intended only for use (after dilution) as a single-dose infusion. When smaller doses are required, the unused portion should be discarded.

Edetate Disodium, USP is chemically designated disodium (ethylenedinitrilo) tetraacetate dihydrate, a white crystalline powder soluble in water. It is also described as the disodium salt of ethylenediamine tetraacetic acid (EDTA) and has the following structural formula:



CLINICAL PHARMACOLOGY

Edetate Disodium Injection, USP forms chelates with the cations of calcium and many divalent and trivalent metals. Because of its affinity for calcium, edetate disodium will produce a lowering of the serum calcium level during intravenous infusion. Slow infusion over a protracted period may cause mobilization of extracirculatory calcium stores. Edetate disodium exerts a negative inotropic effect upon the heart.

After intravenous administration, the chelate formed is excreted in the urine with 50% appearing in 1 hour and over 95% in 24 hours.

Edetate disodium likewise forms chelates with other polyvalent metals and produces increases in urinary excretion of magnesium, zinc and other trace elements. It does not form a chelate with potassium but may reduce the serum level and increase urinary loss of potassium.

INDICATIONS AND USAGE

Endrate (Edetate Disodium Injection, USP) is indicated in selected patients for the emergency treatment of hypercalcemia and for the control of ventricular arrhythmias associated with digitalis toxicity.

CONTRAINDICATIONS

Endrate (Edetate Disodium Injection, USP) is contraindicated in anuric patients. It is not indicated for the treatment of generalized arteriosclerosis associated with advancing age.

WARNINGS

See warning statement, page 1.

Rapid intravenous infusion or attainment of high serum concentration of edetate disodium may cause a precipitous drop in the serum calcium level and may result in fatality. Toxicity appears to be dependent upon both total dosage and speed of administration. The rate of administration and dosage should not exceed that indicated in DOSAGE AND ADMINISTRATION.

Because of its irritant effect on the tissues and because of the danger of serious side effects if administered in the undiluted form, Endrate (Edetate Disodium Injection, USP) should be diluted before infusion. See DOSAGE AND ADMINISTRATION.

PRECAUTIONS

After the infusion of edetate disodium, the patient should remain in bed for a short time because of the possibility of postural hypotension.

The possibility of an adverse effect on myocardial contractility should be considered when administering the drug to patients with heart disease. Caution is dictated in the use of this drug in patients with limited cardiac reserve or incipient congestive failure.

Edetate Disodium Injection, USP therapy should be used with caution in patients with clinical or subclinical potassium deficiency states. In such cases it is advisable to perform serum potassium blood levels for possible hypokalemia and to monitor ECG changes.

The possibility of hypomagnesemia should be kept in mind during prolonged therapy.

Treatment with edetate disodium has been shown to cause a lowering of blood sugar and insulin requirements in patients with diabetes who are treated with insulin.

Do not use unless solution is clear and container is intact. Discard unused portion.

Laboratory Test

Renal excretory function should be assessed prior to treatment. Periodic BUN and creatinine determinations and daily urinalysis should be performed on patients receiving this drug.

Because of the possibility of inducing an electrolyte imbalance during treatment with edetate disodium,

appropriate laboratory determinations and studies to evaluate the status of cardiac function should be performed. Repetition of these tests is recommended as often as clinically indicated, particularly in patients with ventricular arrhythmia and those with a history of seizure disorders or intracranial lesions. If clinical evidence suggests any disturbance of liver function during treatment, appropriate laboratory determinations should be performed and withdrawal of the drug may be required.

Drug/Laboratory Test Interactions

The oxalate method of determining serum calcium tends to give low readings in the presence of edetate disodium; modification of this method, as by acidifying the sample or use of a different method may be required for accuracy. The least interference will be noted immediately before a subsequent dose is administered.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Definitive statements cannot be made due to insufficient data and conflicting information.

Pregnancy Category C: Animal reproduction studies have not been conducted with Edetate Disodium Injection. It is also not known whether Edetate Disodium Injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Edetate Disodium Injection should be given to a pregnant woman only if clearly needed.

Nursing Mothers: The safety of this product in nursing mothers has not been established.

ADVERSE REACTIONS

Gastrointestinal symptoms such as nausea, vomiting and diarrhea are fairly common following administration of this drug. Transient symptoms such as circumoral paresthesia, numbness and headache and a transient drop in systolic and diastolic blood pressure may occur. Thrombophlebitis, febrile reactions; hyperuricemia, anemia, exfoliative dermatitis and other toxic skin and mucous membrane reactions have been reported.

Nephrotoxicity and damage to the reticuloendothelial system with hemorrhagic tendencies have been reported with excessive dosages.

OVERDOSAGE

Because of the possibility that Edetate Disodium Injection, USP may produce a precipitous drop in the serum calcium level, a source of calcium replacement suitable for intravenous administration (such as calcium gluconate) should be instantly available at the bedside before edetate disodium is administered. Extreme caution is dictated in the use of intravenous calcium in the treatment of tetany, especially in digitalized patients because the action of the drug and the replacement of calcium ions may produce a reversal of the desired digitalis effect.

DOSAGE AND ADMINISTRATION

Edetate Disodium Injection, USP is administered by intravenous infusion only after dilution.

For Adults: The recommended daily dosage is 50 mg/kg of body weight to a maximum dose of 3 g in 24 hours. The dose,

calculated by body weight, should be diluted in 500 mL of 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP. The intravenous infusion should be regulated so that three or more hours are required for completion and the cardiac reserve of the patient is not exceeded. A suggested regimen includes five consecutive daily doses followed by two days without medication, with repeated courses as necessary to a total of 15 doses.

For Children: The recommended daily dosage is 40 mg/kg (1 g per 25 kg) of body weight. The dose, calculated by body weight, should be diluted in a sufficient volume of 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP to bring the final concentration of edetate disodium to not more than 3%. The intravenous infusion should be regulated so that three or more hours are required for completion and the cardiac reserve of the patient is not exceeded. The maximum dose is 70 mg/kg per 24-hour period.

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

Drug Interactions

Additives may be incompatible with the reconstituted (diluted) solution required for intravenous infusion. Consult with pharmacist, if available. When introducing additives, use aseptic technique, mix thoroughly and do not store.