New Zealand Datasheet

Name of Medicine

EDETATE DISODIUM INJECTION, USP

Presentation

Edetate Disodium Injection, USP is a sterile, non-pyrogenic, concentrated solution of edetate disodium in water for injection, which, as a result of pH adjustment with sodium hydroxide, contains varying amounts of disodium and trisodium salts. Each ml contains: Edetate Disodium anhydrous 150mg, in Water for Injection q.s. pH is adjusted with Sodium Hydroxide and if necessary Hydrochloric Acid. Approximate pH is 7 (range 6.5 – 7.5).

Uses

Actions

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

Edetate disodium, USP is chemically designated disodium (ethylene-dinitrilo) tetra-acetate dihydrate, a white crystalline powder soluble in water. It is also described as the disodium salt of ethylenediamine-tetra-acetic acid (EDTA).

Edetate disodium injection 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.

Pharmacokinetics

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

Edetate Disodium injection is indicated in selected patients for the emergency treatment of hypercalcemia and for the control of ventricular arrhythmias associated with digitalis toxicity.

Dosage and Administration

Edetate Disodium injection is administered by intravenous infusion only after dilution. 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.

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, or 0.9º/o 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.

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

Contraindications

Edetate Disodium Injection is contraindicated in anuric patients. It is also contraindicated in those persons who have shown hypersensitivity to any component of this preparation.

Warnings and Precautions

FOR INTRAVENOUS INFUSION ONLY AFTER DILUTION

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

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, Edetate Disodium injection should be diluted before infusion, see Dosage and Administration.

After the infusion of Edetate Disodium injection, 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 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.

Carcinogenesis, Mutagenesis, Impairment of Fertility

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

Use in Pregnancy

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 foetal 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.

Use in Lactation

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

Effects on Ability to Drive and Use Machines

No effect expected.

Adverse Effects

Gastrointestinal symptoms such as nausea, vomiting and diarrhoea 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, anaemia, exfoliative dermatitis and other toxic skin and mucous membrane reactions have been reported.

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

Interactions

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.

Overdosage

Because of the possibility that edetate disodium injection 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.

Pharmaceutical Precautions

Store at controlled room temperature 15ºC – 30ºC. Avoid Excessive heat. Protect from freezing.

Medical Classification

Prescription Medicine.

Package Quantities

Edetate Disodium Injection, USP, 150 mg/ml is available in 100 ml vials or 20 ml ampoules.

Further Information

Incompatabilities

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.

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