NOTE. Prussian blue is available in a number of forms and it is not always clear from the literature which form is being referred to. CI Pigment Blue 27 has been used for both insoluble ferric hexacyanoferrate (II) (Colour Index No. 77510) and the soluble potassium, sodium, or ammonium ferric hexacyanoferrate (II) salts

Profile

Prussian blue is used in the treatment of thallium poisoning (see p.2400) and for known or suspected internal contamination with radiocaesium. When given orally it forms a non-absorbable complex with thallium or caesium in the gastrointestinal tract and increases their elimination from the body; it may also bind other elements and patients should be monitored for electrolyte imbalances. Prussian blue may cause constipation and a fibre-based laxative is recommended.

The usual dose of Prussian blue is 250 to 300 mg/kg daily, or up to 20 g daily for an adult, given in divided doses either by mouth or by nasogastric or duodenal tube. In the USA, a lower dose of 3 g three times daily for adults, or 1 g three times daily for children, has been recommended. For thallium poisoning, treatment should continue until the urinary excretion of thallium falls to 500 micrograms or less per 24 hours, the urine or blood concentration is less than 10 micrograms/L, or no thallium can be detected in the faeces. For radiocaesium contamination, a minimum of 30 days treatment should be given.

◊ References.

1. Thompson DF, Church CO. Prussian blue for treatment of radiocesium poisoning. *Pharmacotherapy* 2001; **21:** 1364–7.
2. Hoffman RS. Thallium toxicity and the role of Prussian blue in therapy. *Toxicol Rev* 2003; **22:** 29–40.
3. Thompson DF, Callen ED. Soluble or insoluble Prussian blue for radiocesium and thallium poisoning? *Ann Pharmacother* 2004; **38:** 1509–14.

Preparations

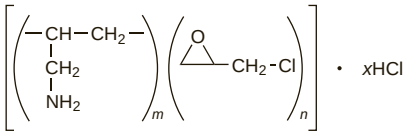
Proprietary Preparations (details are given in Part 3)
Cz.: Radiogardase-Cs; ***Ger.:*** Antidotum Thallii-Heyl; Radiogardase-Cs; ***USA:*** Radiogardase.

Sevelamer *(BAN, rINN)*

Sevelameeri; Sévélamer; Sevelámero; Sevelamerum. Allylamine polymer with 1-chloro-2,3-epoxypropane.

Севеламер

CAS — 52757-95-6.
ATC — V03AE02.
ATC Vet — QV03AE02.



Sevelamer Carbonate *(BANM, USAN, rINNM)*

Carbonato de sevelámero; GT-335-012; Sévélamer Carbonate; Sevelameri Carbonas. Allylamine polymer with 1-chloro-2,3-epoxypropane carbonate.

Севеламера Карбонат

CAS — 845273-93-0.
ATC — V03AE02.
ATC Vet — QV03AE02.

Sevelamer Hydrochloride *(BANM, USAN, rINNM)*

GT16-026A; Hidrocloruro de sevelámero; Sévélamer, Chlorhydrate de; Sevelameri Hydrochloridum. Allylamine polymer with 1-chloro-2,3-epoxypropane hydrochloride.

Севеламера Гидрохлорид

CAS — 182683-00-7.
ATC — V03AE02.
ATC Vet — QV03AE02.

NOTE. The name sevelamer has been used for both sevelamer and sevelamer hydrochloride.

Adverse Effects and Precautions

The most common adverse effects associated with sevelamer are diarrhoea, nausea and vomiting, constipation, headache, cough and other respiratory symptoms, dizziness, hypotension or hypertension, peripheral oedema, pain, and fever. Flatulence, pharyngitis, skin rashes, and pruritus have also occurred; intestinal obstruction and ileus have been reported.

Sevelamer is contra-indicated in patients with hypophosphataemia and in bowel obstruction. Patients with renal impairment may develop hypocalcaemia or hypercalcaemia, and serum-calcium concentrations should be monitored. Serum-chloride concentrations should also be monitored during treatment with sevelamer.

Interactions

Sevelamer has been reported to reduce the bioavailability of ciprofloxacin and should not be taken at the same time. It may also affect the bioavailability of other drugs and should be given at least 3 hours before or 1 hour after drugs for which a reduction in bioavailability could be clinically significant.

Uses and Administration

Sevelamer is a phosphate binder used for hyperphosphataemia in patients with chronic renal failure on haemodialysis. It is given orally as either the carbonate or the hydrochloride. The initial dose is 0.8 to 1.6 g of sevelamer carbonate or sevelamer hydrochloride three times daily with each meal, depending on the severity of hyperphosphataemia. Doses should then be adjusted according to plasma-phosphate concentrations; the usual maintenance dose is from 0.8 to 4 g with each meal.

◊ References.

1. Burke SK. Renagel : reducing serum phosphorus in haemodialysis patients. *Hosp Med* 2000; **61:** 622–7.
2. Qunibi WY, *et al.* Treatment of hyperphosphatemia in hemodialysis patients: The Calcium Acetate Renagel Evaluation (CARE Study). *Kidney Int* 2004; **65:** 1914–26.
3. Almirall J, *et al.* Safety and efficacy of sevelamer in the treatment of uncontrolled hyperphosphataemia of haemodialysis patients. *Nephron Clin Pract* 2004; **97:** c17–c22.
4. Duggal A, *et al.* Novel dosage forms and regimens for sevelamer-based phosphate binders. *J Ren Nutr* 2006; **16:** 248–52.
5. Fischer D, *et al.* Results of a randomized crossover study comparing once-daily and thrice-daily sevelamer dosing. *Am J Kidney Dis* 2006; **48:** 437–44.
6. Suki WN, *et al.* Effects of sevelamer and calcium-based phosphate binders on mortality in hemodialysis patients. *Kidney Int* 2007; **72:** 1130–7.
7. Tonelli M, *et al.* Alberta Kidney Disease Network. Systematic review of the clinical efficacy and safety of sevelamer in dialysis patients. *Nephrol Dial Transplant* 2007; **22:** 2856–66.
8. Ramos R, *et al.* The Catalano–Balear Peritoneal Dialysis Study Group. Sevelamer hydrochloride in peritoneal dialysis patients: results of a multicenter cross-sectional study. *Perit Dial Int* 2007; **27:** 697–701.
9. Delmez J, *et al.* A randomized, double-blind, crossover design study of sevelamer hydrochloride and sevelamer carbonate in patients on hemodialysis. *Clin Nephrol* 2007; **68:** 386–91.
10. Suki WN. Dialysis Clinical Outcomes Revisited Investigators. Effects of sevelamer and calcium-based phosphate binders on mortality in hemodialysis patients: results of a randomized clinical trial. *J Ren Nutr* 2008; **18:** 91–8.
11. Goldsmith DR, *et al.* Sevelamer hydrochloride: a review of its use for hyperphosphataemia in patients with end-stage renal disease on haemodialysis. *Drugs* 2008; **68:** 85–104.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Renagel; ***Belg.:*** Renagel; ***Canad.:*** Renagel; ***Cz.:*** Renagel; ***Denm.:*** Renagel; ***Fin.:*** Renagel; ***Fr.:*** Renagel; ***Ger.:*** Renagel; ***Gr.:*** Renagel; ***Hong Kong:*** Renagel; ***Hung.:*** Renagel; ***Irl.:*** Renagel; ***Israel:*** Renagel; ***Ital.:*** Renagel; ***Jpn:*** Renagel; ***Neth.:*** Renagel; ***Norw.:*** Renagel; ***Pol.:*** Renagel; ***Port.:*** Renagel; ***Spain:*** Renagel; ***Swed.:*** Renagel; ***Switz.:*** Renagel; ***Turk.:*** Renagel; ***UK:*** Renagel; ***USA:*** Renagel; Renvela.

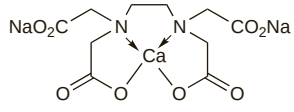
Sodium Calcium Edetate *(BAN, rINN)*

Calcioedetato de sodio; Calcium Disodium Edathamil; Calcium Disodium Edetate; Calcium Disodium Ethylenediaminetetra-acetate; Calcium Disodium Versenate; Calcium édétate de sodium; Calcium EDTA; Disodium Calcium Tetracemate; E385; Edetan sodno-vápenatý hydrát; Edetate Calcium Disodium *(USAN)*; Kalcium-nátrium-edetát; Natrii calcii edetas; Natrii Calcii Edetas Hydricus; Natrio-kalcio edetatas; Natriumkalciumedetat; Natriumkalsiumedetaatti; Sodium, calcium édétate de; Sodium Calciumedetate; Sodu wapnia edetynian; Sodyum Kalsiyum Edetat; Wapniowo-disodowy edetynian. The calcium chelate of disodium ethylenediaminetetra-acetate; Disodium[(ethylenedinitrilo)tetraacetato]calciate(2–) hydrate.

Натрия Кальция Эдетат

$C_{10}H_{12}CaN_2Na_2O_8.xH_2O$ = 374.3 (anhydrous).

CAS — 62-33-9 (anhydrous sodium calcium edetate); 23411-34-9 (sodium calcium edetate hydrate).



NOTE. Do not confuse with sodium edetate; see Inappropriate Administration under Sodium Edetate, p.1464.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *US*, and *Viet.*

Ph. Eur. 6.2 (Sodium Calcium Edetate). A white or almost white, hygroscopic, powder. Freely soluble in water; practically insoluble in alcohol. A 20% solution in water has a pH of 6.5 to 8.0. Store in airtight containers. Protect from light.

USP 31 (Edetate Calcium Disodium). White, slightly hygroscopic, odourless, crystalline powder or granules. Freely soluble in water. pH of a 20% solution in water is between 6.5 and 8.0. Store in airtight containers.

Adverse Effects

Sodium calcium edetate is nephrotoxic and may cause renal tubular necrosis. Nausea, diarrhoea, and abdominal cramp may also occur. Thrombophlebitis has followed intravenous infusion and may be related to the concentration of the injection. Pain at the intramuscular injection site has been reported. Other adverse effects that have been reported include fever, malaise, headache, myalgia, histamine-like responses such as sneezing, nasal congestion, and lachrymation, skin eruptions, transient hypotension, and ECG abnormalities.

Sodium calcium edetate chelates zinc within the body and zinc deficiency has been reported. Displacement of calcium from sodium calcium edetate may lead to hypercalcaemia.

Effects on the kidneys. Of 130 children with lead poisoning who received chelation therapy with sodium calcium edetate (25 mg/kg intramuscularly every 12 hours) and dimercaprol (3 mg/kg intramuscularly every 4 hours) for a total of 5 days, 21 developed clinical evidence of nephrotoxicity and in 4 severe oliguric acute renal failure began 1 or 2 days after chelation therapy was discontinued.[1] Nephrotoxicity was probably attributable to the use of sodium calcium edetate.

1. Moel DI, Kumar K. Reversible nephrotic reactions to a combined 2,3-dimercapto-l-propanol and calcium disodium ethylenediaminetetraacetic acid regimen in asymptomatic children with elevated blood lead levels. *Pediatrics* 1982; **70:** 259–62.

Precautions

Sodium calcium edetate should be used with caution, if at all, in patients with renal impairment. Daily urinalysis to monitor proteinuria and haematuria and regular monitoring of renal and hepatic function has been recommended.

Sodium calcium edetate can chelate several endogenous metals, including zinc, and may increase their excretion; therapy should be intermittent to prevent severe deficiency developing and monitoring of zinc levels may be required (see below).

Sodium calcium edetate should not be given orally in the treatment of lead poisoning as it has been suggested that absorption of lead may be increased as a result.

◊ Sodium calcium edetate 500 mg/m^2 was given by deep intramuscular injection every 12 hours for 5 days to 10 children with asymptomatic lead poisoning.[1] Blood-lead concentrations decreased to about 58% of the pretreatment values after 5 days and were essentially unchanged for up to 60 hours after the last dose. Sodium calcium edetate also produced a marked fall in the mean plasma-zinc concentration but this rebounded rapidly after the end of treatment. Mean urinary-lead excretion increased about 21-fold during the first 24 hours of therapy and urinary-zinc excretion increased about 17-fold. Sodium calcium edetate had little effect on the plasma concentrations or urinary excretion of copper. The results suggested that careful monitoring of zinc was required during treatment with sodium calcium edetate.

1. Thomas DJ, Chisolm JJ. Lead, zinc and copper decorporation during calcium disodium ethylenediamine tetraacetate treatment of lead-poisoned children. *J Pharmacol Exp Ther* 1986; **239:** 829–35.

Pharmacokinetics

Sodium calcium edetate is poorly absorbed from the gastrointestinal tract. It distributes primarily to the extracellular fluid and does not penetrate cells. It is not significantly metabolised; after intravenous injection about 50% of a dose is excreted in the urine in 1 hour and over 95% in 24 hours.

Uses and Administration

Sodium calcium edetate is the calcium chelate of disodium edetate and is a chelator used in the treatment of lead poisoning (see Treatment of Adverse Effects under Lead, p.2332). It mobilises lead from bone and tissues and aids elimination from the body by forming a stable, water-soluble, lead complex which is readily