Dextran 1 (p.1058) may be used to block the formation of dextran-reactive antibodies and hence the hypersensitivity reactions.

Effects on the blood. A syndrome of acute hypotension, pulmonary oedema, coagulopathy, and anaemia, has occurred after the intra-uterine instillation of 32% solution of dextran 70 for hysteroscopy.[1] The volumes of solution that were used in 10 reported cases ranged from 300 to 1200 mL, and these large volumes may have contributed to the intravascular absorption of dextran. The pathogenesis and role of dextran in this syndrome are unclear but suggestions have included acute volume overload, direct alveolar endothelial damage, and release of tissue factors that promote fibrinolysis and a consumptive coagulopathy.

1. Ellingson TL, Aboulafia DM. Dextran syndrome: acute hypotension, noncardiogenic pulmonary edema, anemia, and coagulopathy following hysteroscopic surgery using 32% dextran 70. *Chest* 1997; **111:** 513–18.

Effects on the kidneys. For a report of acute renal failure associated with use of dextran 70, see Dextran 40, above.

Hypersensitivity. In a retrospective study of allergic reactions to dextran 40 and dextran 70 reported in Sweden from 1970 to 1979,[1] there were 478 reports of reactions, 458 of which were considered to be due to dextran, out of 1 365 266 infusions given. There was a male to female ratio of 1.5 to 1 for all reactions and a ratio of 3 to 1 for the most severe reactions. The mean age of the patients was higher in those with severe reactions. Of the 28 fatal reactions, 27 occurred within 5 minutes of the start of the infusion and 25 when less than 25 mL had been infused. Three of the fatal reactions occurred after a test dose of only 0.5 to 1 mL and it was strongly recommended that such test doses should not be used.

An anaphylactic reaction has also been reported[2] more than 75 minutes after intraperitoneal instillation. After successful symptomatic treatment symptoms recurred 20 minutes later, due to slow absorption of dextran from the peritoneal cavity. No further reaction occurred after removal of 200 mL of intraperitoneal fluid by culdocentesis.

Anaphylactoid reactions after BCG vaccination have been attributed to hypersensitivity to dextran in the formulation.[3]

The use of dextran 1 for the prevention of hypersensitivity reactions is discussed under that monograph (p.1058).

1. Ljungström K-G, *et al.* Adverse reactions to dextran in Sweden 1970–1979. *Acta Chir Scand* 1983; **149:** 253–62.
2. Borten M, *et al.* Recurrent anaphylactic reaction to intraperitoneal dextran 75 used for prevention of postsurgical adhesions. *Obstet Gynecol* 1983; **61:** 755–7.
3. Rudin C, *et al.* Anaphylactoid reaction to BCG vaccine containing high molecular weight dextran. *Eur J Pediatr* 1995; **154:** 941–2.

Precautions

Dextran infusions produce a progressive dilution of oxygen-carrying capacity, coagulation factors, and plasma proteins and may overload the circulation. They are therefore contra-indicated in patients with severe heart failure, bleeding disorders such as hypofibrinogenaemia or thrombocytopenia, or renal failure and should be used with caution in patients with renal impairment, haemorrhage, chronic liver disease, or those at risk of developing pulmonary oedema or heart failure. Central venous pressure should be monitored during the initial period of infusion to detect fluid overload. Also patients should be watched closely during the early part of the infusion period, and the infusion stopped immediately if signs of anaphylactic reactions appear. Infusions should also be stopped if there are signs of oliguria or renal failure. The haematocrit should not be allowed to fall below 30% and all patients should be observed for early signs of bleeding complications. The bleeding time may be increased especially in patients receiving large volumes of dextrans. Deficiency of coagulation factors should be corrected and fluid and electrolyte balance maintained. Dehydration should be corrected before or at least during dextran infusions, in order to maintain an adequate urine flow.

The anticoagulant effect of heparin may be enhanced by dextran.

The higher molecular weight dextrans may interfere with blood grouping and cross-matching of blood, while the lower molecular weight dextrans may interfere with some methods. Therefore, whenever possible, a sample of blood should be collected before giving the dextran infusion and kept frozen in case such tests become necessary.

The presence of dextran may interfere with the determination of glucose, bilirubin, or protein in blood.

Pharmacokinetics

After intravenous infusion dextrans with a molecular weight of less than 50 000 are excreted unchanged by the kidney. Dextrans with a molecular weight greater than 50 000 are slowly metabolised to glucose. Small amounts of dextrans are excreted into the gastrointestinal tract and eliminated in the faeces.

About 50% of dextran 70 is excreted unchanged in the urine within 24 hours.

Uses and Administration

Dextran 70 is a plasma volume expander used in the management of hypovolaemic shock (p.1183). As a 6% solution dextran 70 exerts a colloidal osmotic pressure similar to that of plasma proteins and thus produces less expansion of plasma volume than dextrans of a lower molecular weight, although the expansion may have a longer duration because of less rapid renal excretion. Dextran 70 also reduces blood viscosity, interferes with fibrin polymerisation, has an antiplatelet effect, and inhibits sludging or aggregation of red blood cells. It may be used in the prophylaxis of postoperative thromboembolic disorders (p.1189).

Dextran 70 is given by intravenous infusion as a 6% solution, usually in sodium chloride 0.9% or glucose 5%.

Doses depend on the severity of the plasma loss and on the degree of haemoconcentration.

In **shock**, the usual initial dose for rapid expansion of plasma volume is 500 to 1000 mL infused at a rate of 20 to 40 mL/minute. A suggested maximum dose is 20 mL/kg during the first 24-hour period and 10 mL/kg per day thereafter; treatment should not continue for longer than 3 days. Patients may also require blood, coagulation factors, and electrolytes. A hypertonic solution of 6% dextran 70 in sodium chloride 7.5% is also available for use as a plasma expander, given in a single intravenous dose of 250 mL over 2 to 5 minutes, followed by isotonic fluids as required.

For the prophylaxis of pulmonary embolism or venous **thrombosis** in moderate- to high-risk patients undergoing surgery, a dose of 500 to 1000 mL may be given over 4 to 6 hours either during or immediately after surgery. A dose of 500 mL should be given on the next day and in high-risk patients on subsequent alternate days for up to 2 weeks after the operation.

A 32% solution of dextran 70 has been instilled into the uterus in a dose of 50 to 100 mL as a rinsing and dilatation fluid to aid **hysteroscopy**.

Dextran 70 is also an ingredient of artificial tears.

Hypertonic solutions. There is some evidence to suggest that hypertonic solutions of dextran 70 in sodium chloride 7.5% may be an effective treatment option for hypovolaemic shock resulting from trauma.[1,2]

1. Wade CE, *et al.* Efficacy of hypertonic 7.5% saline and 6% dextran-70 in treating trauma: a meta-analysis of controlled clinical studies. *Surgery* 1997; **122:** 609–16.
2. Alpar EK, Killampalli VV. Effects of hypertonic dextran in hypovolaemic shock: a prospective clinical trial. *Injury* 2004; **35:** 500–506.

Preparations

BP 2008: Dextran 70 Intravenous Infusion;
USP 31: Dextran 70 in Dextrose Injection; Dextran 70 in Sodium Chloride Injection.

Proprietary Preparations (details are given in Part 3)
Austral.: Hyskon; ***Braz.:*** Volumax D 70†; ***Canad.:*** Gentran 70; ***Cz.:*** Tensiton†; ***Denm.:*** Macrodex; RescueFlow; ***Fin.:*** RescueFlow; ***Ger.:*** Longasteril 70†; RescueFlow†; ***Israel:*** Macrodex; ***Ital.:*** Plander; Solplex 70†; ***Mex.:*** Macrodex†; ***Neth.:*** RescueFlow; ***Norw.:*** Macrodex; RescueFlow; ***Port.:*** Neodextril 70; RescueFlow; ***S.Afr.:*** Macrodex; RescueFlow; ***Swed.:*** Macrodex; RescueFlow; ***Switz.:*** Dialens; Macrodex†; ***Turk.:*** Macrodex; ***UK:*** Gentran 70; RescueFlow; ***USA:*** Gentran 70; Hyskon; Macrodex; ***Venez.:*** Lacridos; Lacrimart; Lagrimas Artificiales.

Multi-ingredient: ***Arg.:*** Alcon Lagrimas; Kalopsis Lagrimas; Phoenix Lagrimas; Tears Naturale; Visine Plus; ***Austral.:*** Bion Tears; Opti-Free Comfort†; Poly-Tears; Tears Naturale; Visine Advanced Relief; ***Belg.:*** Alcon Adequad; Lacrystat; Tears Naturale; ***Braz.:*** Lacribell; Lacrima Plus; Lacrima†; Trisorb; ***Canad.:*** Artificial Tears; Bion Tears; Tears Naturale; Tears Naturale Forte; Visine Advance Triple Action; ***Chile:*** Lagrimas Artificiales; Naphtears; Nico Drops; Nicotears; Tears Naturale; ***Cz.:*** Tears Naturale; ***Denm.:*** Dacriosol; ***Ger.:*** Isopto Naturale; ***Gr.:*** Tears Naturale; ***Hong Kong:*** Bion Tears; Tears Naturale Forte; ***Hung.:*** Dacrolux; Tears Naturale; ***Indon.:*** Isotic Tearin; Tears; Tears Naturale II; ***Irl.:*** Tears Naturale; ***Israel:*** Tears Naturale; ***Ital.:*** Dacriosol; ***Malaysia:*** Bion Tears; Dacrolux; Tears Naturale; ***Mex.:*** Lacrima Plus; Naphtears; Naturalag; Tears Naturale; Visine Extra; ***Neth.:*** Duratears; ***Norw.:*** Tears Naturale; ***NZ:*** Poly-Tears; Tears Naturale; Visine Advanced Relief; ***Philipp.:*** Gentle Tears; Tears Naturale; ***Pol.:*** Tears Naturale; ***Port.:*** Tears Naturale†; ***Rus.:*** Tears Naturale (Слеза Натуральная); ***S.Afr.:*** Tears Naturale; ***Singapore:*** Bion Tears; Dacrolux†; Tears Naturale; ***Spain:*** Dacrolux; Tears Humectante; ***Swed.:*** Bion Tears; ***Switz.:*** Tears Naturale; ***Thai.:*** Bion Tears; Tears Naturale; ***Turk.:*** Dacrolux; Tears Naturale; ***UK:*** Tears Naturale; ***USA:*** Advanced Relief Visine; Aquasite†; Bion Tears; Lacri-Tears; LubriTears; Moisture Drops; Nature's Tears; Ocucoat; Tears Naturale; Tears Renewed.

Dextran 75 *(BAN, USAN, rINN)* ⊗

Dextrán 75; Dextranum 75.

Декстран 75

CAS — 9004-54-0 (dextran).
ATC — B05AA05.
ATC Vet — QB05AA05.

Profile

Dextran 75 consists of dextrans (glucose polymers) of weight average molecular weight about 75 000 that are derived from the dextrans produced by the fermentation of sucrose by means of a certain strain of *Leuconostoc mesenteroides.*

Dextran 75 is a plasma volume expander with actions and uses similar to dextran 70 (p.1059). It is given by intravenous infusion as a 6% solution in sodium chloride 0.9% or glucose 5%.

Ecallantide *(USAN, rINN)*

DX-88; Ecalantida; Écallantide; Ecallantidum. Human plasma kallikrein-inhibitor (synthetic protein).

Экальлантид

CAS — 460738-38-9.

Profile

Ecallantide is a recombinant inhibitor of human plasma kallikrein. It is under investigation in the management of hereditary angioedema (p.1081).

◊ Reviews.

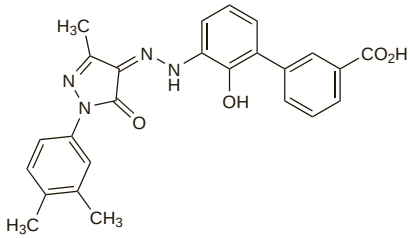
1. Levy JH, O'Donnell PS. The therapeutic potential of a kallikrein inhibitor for treating hereditary angioedema. *Expert Opin Invest Drugs* 2006; **15:** 1077–90.

Eltrombopag *(rINN)*

Eltrombopagum. 3′-{(2*Z*)-2-[1-(3,4-Dimethylphenyl)-3-methyl-5-oxo-1,5-dihydro-4*H*-pyrazol-4-ylidene]diazanyl}-2′-hydroxybiphenyl-3-carboxylic acid.

Элтромбопаг

$C_{25}H_{22}N_4O_4$ = 442.5.
CAS — 496775-61-2.



Eltrombopag Olamine *(USAN, rINNM)*

Eltrombopag olamina; Eltrombopagum Olaminum; SB-497115-GR. 3′-{(2*Z*)-2-[1-(3,4-Dimethylphenyl)-3- methyl-5-oxo-1,5-dihydro-4*H*-pyrazol-4-ylidene]diazanyl}-2′-hydroxybiphenyl-3-carboxylic acid compound with 2-aminoethanol (1:2).

Элтромбопаг Оламин

$C_{25}H_{22}N_4O_4.2(C_2H_7NO)$ = 564.6.
CAS — 496775-62-3.

Profile

Eltrombopag is a non-peptide thrombopoietin receptor agonist. It is under investigation as a platelet growth factor given orally for the management of thrombocytopenia in patients with hepatitis C infection, and in idiopathic thrombocytopenic purpura.

◊ References.

1. McHutchison JG, *et al.* Eltrombopag for thrombocytopenia in patients with cirrhosis associated with hepatitis C. *N Engl J Med* 2007; **357:** 2227–36.
2. Bussel JB, *et al.* Eltrombopag for the treatment of chronic idiopathic thrombocytopenic purpura. *N Engl J Med* 2007; **357:** 2237–47.