available as *The clinical use of blood handbook* at: http://whqlibdoc.who.int/publications/2001/9241545399.pdf (accessed 27/10/05)
4. Cable R, *et al.* American Red Cross practice guidelines for blood transfusion: a compilation from recent peer-reviewed literature (May 2002). Available at: http://www.newenglandblood.org/professional/pgbtscreen.pdf (accessed 27/10/05)
5. Australian Red Cross Blood Service. *Transfusion medicine manual*. Available at: http://www.manual.transfusion.com.au/Home.aspx (accessed 29/08/08)
6. British Committee for Standards in Haematology Transfusion Task Force. Transfusion guidelines for neonates and older children. *Br J Haematol* 2004; **124:** 433–53. Correction. *ibid.* 2007; **136:** 514–16. Also available at: http://www.bcshguidelines.com/pdf/Neonates_124_4_2004.pdf (accessed 27/10/05)
7. McClelland DBL, ed. *Handbook of transfusion medicine: United Kingdom Blood Services*. 4th ed. London: The Stationery Office, 2007. Also available at: http://www.transfusionguidelines.org.uk/docs/pdfs/htm_edition-4_all-pages.pdf (accessed 15/02/07)
8. British Committee for Standards in Haematology. Guidelines on the management of massive blood loss. *Br J Haematol* 2006; **135:** 634–41.
9. Klein HG, *et al.* Red blood cell transfusion in clinical practice. *Lancet* 2007; **370:** 415–26.
10. Council of Europe. *Guide to the preparation, use and quality assurance of blood components.* 13th ed. Strasbourg: Council of Europe Publishing, 2007.

Autologous blood transfusion. Reviews and guidelines have been published on autologous blood transfusion, a procedure where a patient acts as their own blood donor, the blood usually being collected shortly before elective surgery or salvaged during the surgical procedure.[1-6]

1. British Committee for Standards in Haematology Blood Transfusion Task Force. Guidelines for autologous transfusion II: perioperative haemodilution and cell salvage. *Br J Anaesth* 1997; **78:** 768–71. Also available at: http://www.bcshguidelines.com/pdf/bja768.pdf (accessed 27/10/05)
2. Gillon J, Thomas DW. Autologous transfusion. In: Contreras M, ed. *ABC of transfusion*. 3rd ed. London: BMJ Books, 1998: 23–8.
3. Goodnough LT, *et al.* Transfusion medicine: blood conservation. *N Engl J Med* 1999; **340:** 525–33.
4. Vanderlinde ES, *et al.* Autologous transfusion. *BMJ* 2002; **324:** 772–5.
5. Carless P, *et al.* Autologous transfusion techniques: a systematic review of their efficacy. *Transfus Med* 2004; **14:** 123–44.
6. British Committee for Standards in Haematology, Transfusion Task Force. Guidelines for policies on alternatives to allogeneic blood transfusion. 1. Predeposit autologous blood donation and transfusion. *Transfus Med* 2007; **17:** 354–65. Also available at: http://www.bcshguidelines.com/pdf/alt_allogeneic_blood_transfusion.pdf (accessed 09/06/08)

Preparations

USP 31: Whole Blood.

Calcium Alginate

Alginato cálcico; E404.

CAS — 9005-35-0.
ATC — B02BC08.
ATC Vet — QB02BC08.

Profile

Calcium alginate is the calcium salt of alginic acid, a polyuronic acid composed of residues of D-mannuronic and L-guluronic acids. It may be obtained from seaweeds, mainly species of *Laminaria*. Calcium alginate is used as an absorbable haemostatic and for the promotion of wound healing (p.1585); it is also used in the form of a mixed calcium-sodium salt of alginic acid as a fibre made into a dressing or packing material. Calcium ions in the calcium alginate fibres are exchanged for sodium ions in the blood and exudate to form a hydrophilic gel.

Alginic acid and its calcium and sodium salts are widely used in the food industry.

◊ References.

1. Thomas S. Alginate dressings in surgery and wound management–part 1. *J Wound Care* 2000; **9:** 56–60.
2. Thomas S. Alginate dressings in surgery and wound management: part 2. *J Wound Care* 2000; **9:** 115–19.
3. Thomas S. Alginate dressings in surgery and wound management: part 3. *J Wound Care* 2000; **9:** 163–6.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Kaltostat; Nu-Derm Alginato; Tegagen†; ***Austral.:*** Kaltostat†; Melgisorb; Sorbsan†; ***Canad.:*** Algisite†; Kaltostat; Melgisorb; Restore Calci-Care; Tegagen†; ***Fr.:*** Algosteril; Coalgan; Sorbalgon; Stop Hemo; ***Ger.:*** Algosteril†; Urgosorb; ***Gr.:*** Stop Hemo†; ***Irl.:*** Kaltostat; Sorbsan; ***Ital.:*** Algosteril; Cutinova Alginate; Kaltostat; Sorbsan†; ***Port.:*** Sorbsan†; ***S.Afr.:*** Kaltostat; ***UK:*** Algosteril; Comfeel SeaSorb; Kaltostat; Sorbsan; ***USA:*** Calalgin.

Multi-ingredient: ***Arg.:*** Comfeel Plus; Comfeel Purilon†; Comfeel SeaSorb†; Fibracol Plus; Mylanta Reflux; Purilon; Seasorb; ***Canad.:*** Carboflex†; ***Fr.:*** Amiviа†; Askina Sorb†; Clip Hemo; Melgisorb; Purilon; Seasorb; Urgosorb; ***Ger.:*** Algosteril Trionic†; Comfeel Plus; Purilon; SeaSorb Soft; ***Israel:*** Kaltocarb; Kaltostat; ***Port.:*** Askina Sorb†; Carboflex†; Kaltostat; ***UK:*** Comfeel Plus; SeaSorb Soft; ***Venez.:*** Mylanta Plus†.

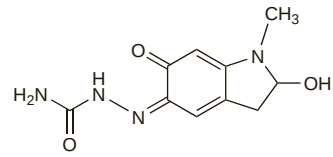
Carbazochrome *(rINN)*

AC-17; Adrenochrome Monosemicarbazone; Carbazochromum; Carbazocromo. 3-Hydroxy-1-methyl-5,6-indolinedione semicarbazone.

Карбазохром

$C_{10}H_{12}N_4O_3$ = 236.2.

CAS — 69-81-8 (carbazochrome); 13051-01-9 (carbazochrome salicylate); 51460-26-5 (carbazochrome sodium sulfonate).
ATC — B02BX02.
ATC Vet — QB02BX02.



Pharmacopoeias. *Jpn* includes Carbazochrome Sodium Sulfonate ($C_{10}H_{11}N_4NaO_5S,3H_2O$ = 376.3).

Profile

Carbazochrome, an oxidation product of adrenaline, has been given as a haemostatic. Carbazochrome sodium sulfonate may be given orally in doses ranging from 30 to 150 mg daily, in at least 3 divided doses. Parenteral doses of 10 mg may be given subcutaneously or intramuscularly, and up to 100 mg may be given intravenously. It has also been given as the dihydrate and as the salicylate.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Adrenoplasma†; Adrenoxil†; ***Ger.:*** Adrenoxyl†; ***Hong Kong:*** Adona; ***India:*** Sigmachrome; Siochrome; Styptocid; ***Indon.:*** Adona; Adrome; ***Ital.:*** Adona; ***Jpn:*** Adona; ***Port.:*** Adrenoxil; ***Thai.:*** Neo-Hesna.

Multi-ingredient: ***India:*** Cadisper C; CKP; Siochrome; Styptocid; Styptocip†; ***Ital.:*** Fleboside; ***Mex.:*** Hemosin-K; ***Spain:*** Cromoxin K†; Flebeside†; Perfus Multivitaminico; ***Venez.:*** Dremo-K†.

Darbepoetin Alfa *(BAN, USAN, rINN)* ⊗

Darbepoetiinialfa; Darbepoetina alfa; Darbépoétine Alfa; Darbepoetinum Alfa; NESP; Novel Erythropoiesis Stimulating Protein. 30-L-Asparagine-32-L-threonine-87-L-valine-88-L-asparagine-90-L-threoninеerythropoietin (human).

Дарбепоетин Альфа

CAS — 209810-58-2.
ATC — B03XA02.
ATC Vet — QB03XA02.

Adverse Effects and Precautions

As for Epoetins, p.1061.

Pharmacokinetics

On subcutaneous injection the bioavailability of darbepoetin alfa is about 37% and absorption is slow. It undergoes extensive metabolism, with terminal half-lives of 21 and 49 hours after intravenous and subcutaneous use respectively.

◊ References.

1. Heatherington AC, *et al.* Pharmacokinetics of novel erythropoiesis stimulating protein (NESP) in cancer patients: preliminary report. *Br J Cancer* 2001; **84** (suppl): 11–16.
2. Allon M, *et al.* Pharmacokinetics and pharmacodynamics of darbepoetin alfa and epoetin in patients undergoing dialysis. *Clin Pharmacol Ther* 2002; **72:** 546–55.
3. Lerner G, *et al.* Pharmacokinetics of darbepoetin alfa in pediatric patients with chronic kidney disease. *Pediatr Nephrol* 2002; **17:** 933–7.
4. Heatherington AC, *et al.* Pharmacokinetics of darbepoetin alfa after intravenous or subcutaneous administration in patients with non-myeloid malignancies undergoing chemotherapy. *Clin Pharmacokinet* 2006; **45:** 199–211.

Uses and Administration

Darbepoetin alfa is an analogue of the endogenous protein hormone erythropoietin with similar properties to the epoetins (p.1062). It is used in the management of anaemia associated with chronic renal failure (see Normocytic-normochromic Anaemia, p.1044) and for anaemia caused by chemotherapy in patients with non-myeloid malignancies.

For **anaemia associated with chronic renal failure** in adults and children aged 11 years and older, the aim of treatment is to increase the haemoglobin concentration to 10 to 12 g per 100 mL. The rate of rise in haemoglobin should be gradual to minimise adverse effects such as hypertension; a rate not exceeding 2 g per 100 mL per month is suggested. Darbepoetin alfa is given by subcutaneous or intravenous injection in an initial dose of 450 nanograms/kg once weekly, as a single injection. In patients on haemodialysis, the intravenous route is recommended to reduce the risk of developing neutralising antibodies and pure red cell aplasia (see Effects on the Blood under Epoetins, p.1061). The dose should be adjusted at intervals of not less than 4 weeks, according to response, until the target haemoglobin concentration is achieved. In general, adjustments are made by increasing or decreasing the dose by about 25%. Maintenance doses may then be continued once weekly. Patients may be converted from weekly doses to once every 2 weeks, and should receive a dose that is equal to twice the dose that had been given once weekly. Alternatively, for patients who are not on dialysis, an initial dose of 750 nanograms/kg subcutaneously once every 2 weeks may be used, followed by dose adjustment. When the target haemoglobin concentration is achieved, a maintenance dose may be given once a month; this is equal to twice the dose that had been given once every 2 weeks.

For **anaemia in chemotherapy patients** with non-myeloid malignancies, darbepoetin alfa is given subcutaneously in an initial dose of 500 micrograms (6.75 micrograms/kg) once every 3 weeks; if the response is inadequate after 9 weeks, further therapy with darbepoetin alfa may not be effective. Alternatively, it may be given in an initial dose of 2.25 micrograms/kg once weekly. If the response is inadequate after 6 weeks, the dose may be increased to 4.5 micrograms/kg once weekly. Darbepoetin alfa should be stopped after the course of chemotherapy has finished, but it may be continued for up to 4 weeks in the UK. The rate of rise in haemoglobin should be gradual; a rate not exceeding 2 g per 100 mL per month, and a target haemoglobin of not more than 12 g per 100 mL, are suggested. Once the desired haemoglobin target has been reached, the dose should be reduced by 25 to 50% to maintain that level.

◊ Reviews.

1. Ibbotson T, Goa KL. Darbepoetin alfa. *Drugs* 2001; **61:** 2097–2104.
2. The NESP Usage Guidelines Group. Practical guidelines for the use of NESP in treating renal anaemia. *Nephrol Dial Transplant* 2001; **16** (suppl 3): 22–8.
3. Overbay DK, Manley HJ. Darbepoetin-α: a review of the literature. *Pharmacotherapy* 2002; **22:** 889–97.
4. Joy MS. Darbepoetin alfa: a novel erythropoiesis-stimulating protein. *Ann Pharmacother* 2002; **36:** 1183–92.
5. Cvetkovic RS, Goa KL. Darbepoetin alfa in patients with chemotherapy-related anaemia. *Drugs* 2003; **63:** 1067–74.
6. Siddiqui MAA, Keating GM. Darbepoetin alfa: a review of its use in the treatment of anaemia in patients with cancer receiving chemotherapy. *Drugs* 2006; **66:** 997–1012.

Preparations

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

Dextran 1 *(BAN, rINN)* ⊗

Dekstraani 1; Dekstranas 1; Dextrán 1; Dextranum 1.

Декстран 1

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

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*

Ph. Eur. 6.2 (Dextran 1 for Injection). A low-molecular-weight fraction of dextran, consisting of a mixture of isomalto-oligosaccharides. It is obtained by hydrolysis and fractionation of dextrans produced by fermentation of sucrose using a certain strain or substrains of *Leuconostoc mesenteroides*. The average relative molecular mass is about 1000.

A white or almost white, hygroscopic powder. Very soluble in water; very slightly soluble in alcohol.

USP 31 (Dextran 1). A low-molecular-weight fraction of dextran, consisting of a mixture of isomalto-oligosaccharides. It is obtained by controlled hydrolysis and fractionation of dextrans produced by fermentation of certain strains of *Leuconostoc mesenteroides*, in the presence of sucrose. It is a glucose polymer in