those who were not septic and had received unfiltered packed red cells. Mean white cell counts were increased significantly 2 hours after infusion, remained elevated for about 12 hours, and returned to baseline by 24 hours. In 11 patients who required more than one transfusion, the use of filtered packed red cells was not associated with leucocytosis. Concentrations of interleukin-8 were found to be raised in unfiltered blood after 4 weeks of storage, and were higher in the transfused blood that caused leucocytosis. The authors suggested that cytokines produced by leucocytes in stored blood might be responsible for leucocytosis in recipients of unfiltered packed red cells.

1. Fenwick JC, *et al.* Blood transfusion as a cause of leucocytosis in critically ill patients. *Lancet* 1994; **344:** 855–6.
2. Izbicki G, *et al.* Transfusion-related leukocytosis in critically ill patients. *Crit Care Med* 2004; **32:** 439–42.

Effects on the lungs. A rare but life-threatening complication of transfusion of blood or other plasma-containing products is acute lung injury, often termed transfusion-related acute lung injury (TRALI). Symptoms develop during or within 6 hours of infusion and are those of acute respiratory distress syndrome[1-3] (p.1498). Treatment is the same as for acute respiratory distress of any cause but oxygen exchange usually begins to improve between 24 and 48 hours; if the patient survives there appear to be no long-term sequelae.[1] The presence of HLA-specific antileucocyte antibodies in plasma from multiparous female donors appears to play a role in starting the reaction;[1,3] such antibodies have also been identified in some implicated male donors.[2] Another mechanism, the neutrophil priming hypothesis, proposes that TRALI results from 2 independent events. The first event causes the recipient's neutrophils to be primed and is related to the recipient's condition; in the second event the infused blood product activates the primed neutrophils in the lung, which causes endothelial damage.[2,3]

1. Wallis JP. Transfusion-related acute lung injury (TRALI)—under-diagnosed and under-reported. *Br J Anaesth* 2003; **90:** 573–6.
2. Holness L, *et al.* Fatalities caused by TRALI. *Transfus Med Rev* 2004; **18:** 184–8.
3. Kleinman S, *et al.* Toward an understanding of transfusion-related acute lung injury: statement of a consensus panel. *Transfusion* 2004; **44:** 1774–89.

Graft-versus-host disease. Acute graft-versus-host disease (see Haematopoietic Stem Cell Transplantation, p.1811) has been reported in both immunocompromised and immunocompetent patients after blood transfusion.[1] Symptoms include fever, rash, abnormal liver function tests, diarrhoea, and pronounced leucopenia and pancytopenia. The reaction can be severe and fatal.

High-risk immunocompromised groups include bone marrow transplant recipients, patients with congenital immunodeficiencies, fetuses receiving intra-uterine transfusions, patients with Hodgkin's disease, and patients treated with purine analogue drugs such as fludarabine. Patients at less risk include those with acute leukaemia, non-Hodgkin's lymphoma, solid tumours treated with intensive chemotherapy or radiotherapy, premature infants and those undergoing exchange transfusion, and solid organ transplant recipients.

Immunocompetent patients who share an HLA haplotype with HLA-homozygous blood donors also appear to be at increased risk. Such cases have been reported particularly in Japan, where practices have included the use of transfusions from blood relatives. There is also a high incidence of shared haplotype in the population.

Infusion of products containing viable lymphocytes appears to be responsible. Treatment of graft-versus-host disease associated with transfusion is largely ineffective and patients considered to be at risk should be given products depleted of viable lymphocytes by irradiation. Blood products depleted of leucocytes by filtration still contain a small percentage of viable leucocytes, and this should not be used as the sole method to prevent graft-versus-host disease.

1. Schroeder ML. Transfusion-associated graft-versus-host disease. *Br J Haematol* 2002; **117:** 275–87.

Malignant neoplasms. It has been suggested that perioperative allogeneic blood transfusion is associated with an increase in the risk of recurrence, and decreased long-term survival, after resection of malignancy. This suggestion was based on retrospective observational studies, and was attributed to immunosuppressant effects of allogeneic blood. Randomised controlled trials have produced conflicting results, but a 1996 review[1] did not find a detrimental effect on the risk of cancer recurrence, and suggested that the findings of the observational studies probably resulted from the confounding effect of factors associated with the need for transfusion. A later meta-analysis[2] of 32 studies of perioperative transfusion in patients undergoing colorectal surgery concluded that the cancer recurrence rate was increased (odds ratio 1.68) in patients given transfusions. Risk factors associated with this increase were rectal disease, more advanced disease, and an increased number of transfused units. However, many of the included studies had small sample sizes, there was significant heterogeneity, and other possible surgery-related risk factors could not be evaluated, such that a causal association between the increased risk of cancer recurrence and transfusion could not be established. Other systematic reviews have come to different conclusions. A meta-analysis[3] of studies in patients undergoing resection of any type of solid tumour included only studies that used an active comparator (leucocyte-depleted or autologous blood). Only 8 studies met the inclusion criteria and the analysis provided no evidence of an increased risk of death or cancer recurrence in patients given allogeneic blood. The proposed detrimental immunosuppressive effect of perioperative allogeneic blood transfusion was studied in colorectal cancer patients given either allogeneic packed red cells (buffy coat removed) or leucocyte-depleted red cells.[4] Although the leucocyte count is reduced when the buffy coat is removed, more leucocytes are removed from leucocyte-depleted red cells, which should reduce any immunosuppressive effect. However, after 5 years there was no difference in survival or recurrence rates between the two groups. Survival was better for a third group of non-transfused patients, but this may be explained by a higher incidence of rectal cancer in the transfused groups, and the better clinical status of patients not requiring transfusion. A review[5] of individual studies and meta-analyses concluded that a causal relationship between allogeneic blood transfusion and solid cancer recurrence had not been proven. There was some evidence for transfusion-associated immunomodulation, but the mechanisms of effect and the specific constituents of allogeneic blood that mediate the effect remain unclear.

Epidemiological studies have reported an increase in the incidence of non-Hodgkin's lymphoma coinciding with the increase in the use of allogeneic blood transfusions since the 1950s. Proposed mechanisms have included transfusion-associated immunosuppression, transmission of oncogenic viruses, and blood donation by prelymphomatous donors.[6,7] Although some case-control studies have reported no association between blood transfusion and the development of non-Hodgkin's lymphoma,[8,9] others have reported a positive association, particularly for some subtypes of lymphoma.[10] Reviews[6,7] of these and other studies have found considerable disagreement between reports. This may result from biases in study design, confounding factors such as HIV infection, and lack of consensus on lymphoma classification.

1. Vamvakas EC. Transfusion-associated cancer recurrence and postoperative infection: meta-analysis of randomized, controlled clinical trials. *Transfusion* 1996; **36:** 175–86.
2. Amato AC, Pescatori M. Effect of perioperative blood transfusions on recurrence of colorectal cancer: meta-analysis stratified on risk factors. *Dis Colon Rectum* 1998; **41:** 570–85.
3. McAlister FA, *et al.* Perioperative allogeneic blood transfusion does not cause adverse sequelae in patients with cancer: a meta-analysis of unconfounded studies. *Br J Surg* 1998; **85:** 171–8.
4. van de Watering LMG, *et al.* Perioperative blood transfusions, with or without allogeneic leucocytes, relate to survival, not to cancer recurrence. *Br J Surg* 2001; **88:** 267–72.
5. Vamvakas EC, Blajchman MA. Deleterious clinical effects of transfusion-associated immunomodulation: fact or fiction? *Blood* 2001; **97:** 1180–95.
6. Vamvakas EC. Allogeneic blood transfusion as a risk factor for the subsequent development of non-Hodgkin's lymphoma. *Transfus Med Rev* 2000; **14:** 258–68.
7. Chow EJ, Holly EA. Blood transfusions and non-Hodgkin's lymphoma. *Epidemiol Rev* 2002; **24:** 269–79.
8. Maguire-Boston EK, *et al.* Blood transfusion and risk of non-Hodgkin's lymphoma. *Am J Epidemiol* 1999; **149:** 1113–18.
9. Chow EJ, Holly EA. Blood transfusions as a risk factor for non-Hodgkin's lymphoma in the San Francisco Bay Area: a population-based study. *Am J Epidemiol* 2002; **155:** 725–31.
10. Cerhan JR, *et al.* Blood transfusions and risk of non-Hodgkin's lymphoma subtypes and chronic lymphocytic leukemia. *Cancer Epidemiol Biomarkers Prev* 2001; **10:** 361–8.

Precautions

Whole blood should generally not be transfused unless the ABO and Rh groups of the patient's and the donor's blood have been verified and a compatibility check made between the patient's serum and the donor's red cells (see under Blood Groups, below).

The Rh group of the recipient should always be determined and ideally all patients should be transfused with blood of homologous Rh groups.

To reduce the possibility of cardiac arrest from cardiac hypothermia when large volumes are used or the blood is transfused rapidly, and to minimise postoperative shivering, stored blood should be carefully warmed to about 37° before transfusion.

Whole blood should not be given to patients with chronic anaemia who have a normal or elevated plasma volume.

Drugs should *not* be added to blood.

Transfusion of blood from donors who have recently been receiving drug treatment may be hazardous to the recipient.

◊ Guidelines[1-4] for accepting blood from donors who have been receiving drugs have been published.

1. Ferner RE, *et al.* Drugs in donated blood. *Lancet* 1989; **ii:** 93–4.
2. Stichtenoth DO, *et al.* Blood donors on medication: are deferral periods necessary? *Eur J Clin Pharmacol* 2001; **57:** 433–40.
3. UK Blood Transfusion Services. Whole blood and components donor selection guidelines: drug index (revised 23/04/08). Available at: http://www.transfusionguidelines.org.uk/index.asp?Publication=DI&Section=4 (accessed 29/08/08)
4. American Red Cross. Blood donation eligibility guidelines (revised 08/05/08). Available at: http://www.redcross.org/services/biomed/0,1082,0_557_,00.html#med (accessed 29/08/08)

Abuse. References to the infusion of whole blood or packed red blood cells to enhance athletic performance.[1,2]

1. Ekblom BT. Blood boosting and sport. *Baillieres Best Pract Res Clin Endocrinol Metab* 2000; **14:** 89–98.
2. Leigh-Smith S. Blood boosting. *Br J Sports Med* 2004; **38:** 99–101.

Blood groups. The chief blood group systems are the ABO system and the Rhesus system.

In simple terms red blood cells carry on their surface genetically determined antigens. A person with antigen A, B, A plus B, or neither is classified as group A, B, AB, or O respectively. Such persons will have, in their serum, antibodies to B, A, neither, or both respectively—anti-B (β), anti-A (α), or anti-B plus anti-A (α + β). Giving blood containing red cells from a person of group A to a person with anti-A results in agglutination or possibly haemolysis. For the determination of the ABO group the agglutinogens of the red cells and the agglutinins of the serum are determined by testing against known standards.

In the Rhesus system many persons carry an antigen (Rh-positive) which stimulates antibody formation in Rh-negative persons; subsequent exposure to Rh-positive blood causes haemolysis.

Many variants of these and other systems, are recognised.

Uses and Administration

Blood is a complex fluid with many functions including the maintenance of hydration of the tissues, maintenance of body temperature, and the transport within the body of gases, ions, nutrients, hormones, enzymes, antibodies, waste products of metabolism, and drugs.

The main components of blood are plasma, red blood cells (erythrocytes), white blood cells (leucocytes), and platelets (for further information on different blood cells and their formation, and average counts in adults, see Haematopoiesis, p.1042). Serum is the fluid which remains once blood or plasma has clotted; it is, in effect, plasma with fibrinogen removed.

Whole blood is used as a source of red cell concentrates, clotting factors, platelets, plasma and plasma fractions, and immunoglobulins, each of which has specific indications for use. Because of the risks involved in transfusing whole blood and the need for economy in its use, the appropriate blood component should be used whenever possible.

Whole blood may be used where replacement of plasma proteins as well as red blood cells is needed, for example after acute blood loss during surgery or severe haemorrhage. It may also be used to supplement the circulation during cardiac bypass surgery.

The amount of whole blood transfused and the rate at which it is given depend upon the patient's age and general condition, upon the state of their circulatory system, and upon the therapeutic indication for transfusion.

The expression 'unit of blood' generally represents a volume of about 510 mL, including anticoagulant. For blood preparations a unit generally refers to the quantity of a blood component obtained from 1 unit of whole blood. Specific units of activity are used for some blood components.

The haemoglobin concentration of the blood of the average adult is raised by about 1 g per 100 mL by the transfusion of 1 unit of whole blood.

◊ Reviews and guidelines for the use of blood and blood components.

1. Contreras M, ed. *ABC of transfusion.* 3rd ed. London: BMJ Books, 1998.
2. Goodnough LT, *et al.* Transfusion medicine: blood transfusion. *N Engl J Med* 1999; **340:** 438–47.
3. World Health Organization. *The clinical use of blood in medicine, obstetrics, paediatrics, surgery and anaesthesia, trauma and burns.* Geneva: World Health Organization, 2001. Also

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†.

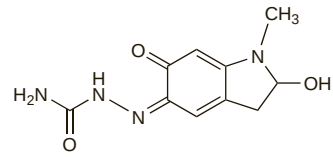
Carbazochrome *(rINN)*

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