Use of leucocyte-depleted platelet concentrates reduces the incidence of transfusion reactions and of HLA sensitisation. Platelet concentrates prepared from Rh(D)-positive donors should generally not be given to Rh(D)-negative women of child-bearing potential. Ideally platelet concentrates should also be ABO-compatible with the recipient.

ABO compatibility. Platelets express the ABO blood group antigens and the plasma component of platelet concentrates may contain alloantibodies from the donor (see Blood Groups, p.1057). Ideally, ABO-identical platelet concentrates should be used, but ABO-compatible concentrates are often used and incompatible concentrates may be used in an emergency. However, the use of ABO-mismatched platelets can reduce the efficacy of the platelet transfusion. Also, acute haemolytic reactions can occur after infusion of mismatched platelets if the infused plasma contains high antibody titres or the volume of plasma infused is large. Some have suggested that screening donors for high antibody titres should be routine in order to avoid this, but there is no consensus as to the definition of critical titre. There have been mixed reports on whether the use of ABO-mismatched platelets has an effect on the recipient's long-term clinical course.

Reviews.

1. Lozano M, Cid J. The clinical implications of platelet transfusions associated with ABO or Rh(D) incompatibility. *Transfus Med Rev* 2003; **17:** 57–68.

HLA antibodies. Platelets obtained from single donors have been used in patients receiving multiple transfusions of platelet concentrates to reduce the formation of antibodies to HLA. Some practitioners suggest[1] that patients who are likely to need long-term platelet support should be typed for HLA A and B antigens and screened for HLA antibodies. Leucocyte-depleted platelets and UVB-irradiated platelets have also been tried. A study[2] in 530 patients found that the incidence of platelet refractoriness was reduced from 13% of those patients receiving pooled platelet concentrates to 3% and 5% of those receiving leucocyte-depleted and UVB-irradiated platelets, respectively. A meta-analysis[3] of this and earlier small studies also concluded that leucocyte depletion reduced the risk of alloimmunisation and platelet refractoriness. Some guidelines[4] have nonetheless considered that there is no convincing evidence of clinical benefit from routine use.

1. Dan ME, Schiffer CA. Strategies for managing refractoriness to platelet transfusions. *Curr Hematol Rep* 2003; **2:** 158–64.
2. The Trial to Reduce Alloimmunization to Platelets Study Group. Leukocyte reduction and ultraviolet B irradiation of platelets to prevent alloimmunization and refractoriness to platelet transfusions. *N Engl J Med* 1997; **337:** 1861–9.
3. Vamvakas EC. Meta-analysis of randomized controlled trials of the efficacy of white cell reduction in preventing HLA-alloimmunization and refractoriness to random-donor platelet transfusions. *Transfus Med Rev* 1998; **12:** 258–70.
4. British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines on the clinical use of leucocyte-depleted blood components. *Transfus Med* 1998; **8:** 59–71. Also available at: http://www.bcshguidelines.com/pdf/trans129.pdf (accessed 27/10/05)

Uses and Administration

Blood platelets assist in the haemostatic process (p.1045) by aggregating to form a platelet thrombus, and by releasing factors involved in initiating coagulation.

Transfusions of platelet concentrates are given to patients with thrombocytopenic haemorrhage (see p.1051). They are also given prophylactically to reduce the frequency of haemorrhage in thrombocytopenia associated with the chemotherapy of neoplastic disease (see p.640).

◊ References.

1. Fresh-frozen Plasma, Cryoprecipitate, and Platelets Administration Practice Guidelines Development Task Force of the College of American Pathologists. Practice parameter for the use of fresh-frozen plasma, cryoprecipitate, and platelets. *JAMA* 1994; **271:** 777–81.
2. Brozović B, *et al.* Platelet and granulocyte transfusions. In: Contreras M, ed. *ABC of transfusion.* 3rd ed. London: BMJ Books, 1998: 17–22.
3. Schiffer CA, *et al.* Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology. *J Clin Oncol* 2001; **19:** 1519–38. Also available at: http://www.jco.org/cgi/reprint/19/5/1519.pdf (accessed 27/10/05)
4. British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the use of platelet transfusions. *Br J Haematol* 2003; **122:** 10–23. Also available at: http://www.bcshguidelines.com/pdf/platelettrans040703.pdf (accessed 27/10/05)
5. Heal JM, Blumberg N. Optimizing platelet transfusion therapy. *Blood Rev* 2004; **18:** 149–65.
6. Stroncek DF, Rebulla P. Platelet transfusions. *Lancet* 2007; **370:** 427–38.

Preparations

USP 31: Platelet Concentrate; Platelets.

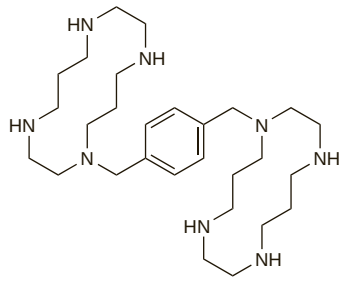
Plerixafor *(USAN, rINN)*

AMD-3100; JM-3100; Plérixafor; Plerixaforum; SDZ-SID-791; SID-791. 1,1′-(1,4-Phenylenebismethylene)bis(1,4,8,11-tetraazacyclotetradecane).

Плериксафор

$C_{28}H_{54}N_8$ = 502.8.

CAS — 110078-46-1 (plerixafor); 155148-31-5 (plerixafor hydrochloride).



Profile

Plerixafor is a CXCR4 receptor antagonist. It is under investigation for the mobilisation of haematopoietic stem cells for collection and subsequent autologous or allogeneic transplantation.

Policresulen *(rINN)*

Acidum Metacresolsulfonicum c. Formaldehydo; *m*-Cresolsulphonic acid-formaldehyde condensation product; Dicresulene polymer; Dihydroxydimethyldiphenylmethanedisulphonic acid polymer; Formaldehydhaltig Metakresolsulfonsyra; Formaldehydipitoinen Metakresolisulfonihappo; Metacresolsulfonic Acid-Formaldehyde; Metacresolsulphonic Acid-Formaldehyde; Methylenebis(hydroxytoluenesulphonic acid) polymer; Policrésulène; Policresuleno; Policresulenum; Polikresuleeni; Polikresulen; Polímero de dicresuleno; Polycresolsulfonate. α-(4-Hydroxy-2-methyl-5-sulfobenzyl)-ω-(4-hydroxy-5-sulfo-*o*-tolyl)poly[(4-hydroxy-2-methyl-5-sulfo-*m*-phenylene)methylene]; 2-Hydroxy-*p*-toluenesulfonic acid, polymer with formaldehyde.

Поликрезулен

$(C_8H_9O_4S)(C_8H_8O_4S)_n(C_7H_7O_4S)$.

CAS — 9011-02-3; 101418-00-2.

ATC — D08AE02; G01AX03.

ATC Vet — QD08AE02; QG01AX03; QG51AD02.

Profile

Policresulen is used as a topical haemostatic and antiseptic. It is also used similarly in veterinary medicine.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Albocresil; ***Braz.:*** Albocresil; ***Chile:*** Albocresil†; ***Cz.:*** Vagothyl; ***Fr.:*** Negatol†; ***Ger.:*** Albothyl; ***Hong Kong:*** Albothyl; ***Hung.:*** Vagothyl; ***Indon.:*** Albothyl; ***Ital.:*** Emaftol; Negatol; ***Malaysia:*** Albothyl; ***Mex.:*** Albothyl; ***Philipp.:*** Albothyl; ***Pol.:*** Albothyl; Vagothyl; ***Port.:*** Nelex; ***Rus.:*** Vagothyl (Ваготил); ***S.Afr.:*** Nelex†; ***Singapore:*** Albothyl; ***Switz.:*** Negatol; Negatol Dental.

Multi-ingredient: ***Arg.:*** Proctyl; ***Braz.:*** Proctyl; ***Cz.:*** Faktu; ***Fin.:*** Faktu†; ***Ger.:*** Faktu; ***Hong Kong:*** Faktu; ***Indon.:*** Faktu; ***Mex.:*** Proctoacid; ***Philipp.:*** Faktu; ***Port.:*** Faktu; ***Singapore:*** Faktu†; ***Switz.:*** Faktu.

Polygeline *(BAN, pINN)* ⊗

Poligelina; Polygéline; Polygelinum.

Полигелин

CAS — 9015-56-9.

ATC — B05AA10.

Description. Polygeline is a polymer prepared by cross-linking polypeptides derived from denatured gelatin with a di-isocyanate to form urea bridges.

Incompatibility. Intravenous preparations of polygeline contain calcium ions and are incompatible with citrated blood.

Adverse Effects

As for Gelatin, p.1072.

Hypersensitivity. Fatal reactions after polygeline infusion have been reported in 2 patients with bronchial asthma.[1,2] Both patients were undergoing epidural analgesia with bupivacaine and polygeline was given to correct hypotension that had not responded to infusion of crystalloids. One patient developed focal seizures.[2] Both patients developed refractory bronchospasm and cardiac arrhythmias and died despite intensive resuscitation attempts.

Licensed drug information recommends that prophylaxis with histamine H_1- and H_2-antagonists should be given to patients with known allergic conditions such as asthma. Similar advice has been offered[3] for patients undergoing anaesthesia and receiving polygeline following findings of an increased incidence of severe histamine-related reactions in such patients. Nevertheless, severe respiratory distress developed in an asthmatic patient given polygeline under spinal anaesthesia despite premedication with bronchodilators and antihistamines.[4]

There is a possibility of cross reactivity between polygeline and succinylated gelatin (see Gelatin, p.1072).

1. Freeman MK. Fatal reaction to haemaccel. *Anaesthesia* 1979; **34:** 341–3.
2. Barratt S, Purcell GJ. Refractory bronchospasm following "Haemaccel" infusion and bupivacaine epidural anaesthesia. *Anaesth Intensive Care* 1988; **16:** 208–11.
3. Lorenz W, *et al.* Incidence and clinical importance of perioperative histamine release: randomised study of volume loading and antihistamines after induction of anaesthesia. *Lancet* 1994; **343:** 933–40.
4. Kathirvel S, *et al.* Severe life threatening reaction to Haemaccel in a patient with bronchial asthma. *Eur J Anaesthesiol* 2001; **18:** 122–3.

Precautions

Precautions that should be observed with plasma expanders are described under Dextran 70, p.1060, and should be considered when polygeline is used for this purpose.

Polygeline preparations contain calcium ions and therefore should be used with caution in patients being treated with cardiac glycosides.

Pharmacokinetics

Like gelatin, polygeline is excreted mainly in the urine. The half-life is about 5 to 8 hours.

Renal impairment. In a study[1] in 52 patients with normal or impaired renal function given 500 mL of polygeline 3.5% about 50% of the dose was excreted in the urine within 48 hours in those with normal renal function. Excretion of polygeline in those with renal impairment, based on the patient's glomerular filtration rate (GFR), was found to be:

- GFR 31 to 90 mL/minute: unimpaired
- GFR 11 to 30 mL/minute: slightly reduced
- GFR 2 to 10 mL/minute: reduced to 27% in 48 hours
- GFR 0.5 to 2 mL/minute: reduced to 9.3% in 48 hours

The mean half-life of the elimination phase was 505 minutes in those with adequate renal function, increasing to 985 minutes in those with end-stage renal failure. Polygeline 500 mL of 3.5% solution could be given twice weekly for 1 to 2 months even in patients with total anuria.

1. Köhler H, *et al.* Elimination of hexamethylene diisocyanate cross-linked polypeptides in patients with normal or impaired renal function. *Eur J Clin Pharmacol* 1978; **14:** 405–12.

Uses and Administration

Polygeline is a plasma volume expander used as a 3.5% solution with electrolytes in the management of hypovolaemic shock (p.1183). The rate of infusion depends on the condition of the patient and does not normally exceed 500 mL in 60 minutes although it may be greater in emergencies. Initial doses for hypovolaemic shock usually consist of 500 to 1000 mL; up to 1500 mL of blood loss can be replaced by polygeline alone. Patients losing greater volumes of blood will require blood transfusion as well as plasma expanders.

Polygeline is also used in extracorporeal perfusion fluids, as a perfusion fluid for isolated organs, as fluid replacement in plasma exchange, and as a carrier solution for insulin. For plasma exchange, up to 2 litres of polygeline may be given as sole replacement fluid.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Haemaccel†; ***Austral.:*** Haemaccel; ***Austria:*** Haemaccel; ***Belg.:*** Haemaccel†; ***Braz.:*** Haemaccel; ***Chile:*** Haemaccel†; ***Cz.:*** Haemaccel†; ***Ger.:*** Haemaccel; ***Gr.:*** Haemaccel†; ***Hong Kong:*** Haemaccel†; ***India:*** Haemaccel; ***Indon.:*** Haemaccel; ***Irl.:*** Haemaccel†; ***Israel:*** Haemaccel†; ***Ital.:*** Emagel; Gelplex; ***Malaysia:*** Haemaccel†; ***Mex.:*** Haemaccel; Phygelin; ***Neth.:*** Haemaccel; ***Norw.:*** Haemaccel†; ***NZ:*** Haemaccel; ***Port.:*** Haemaccel; ***S.Afr.:*** Haemaccel; ***Singapore:*** Haemaccel; ***Switz.:*** Haemaccel†; ***Thai.:*** Haemaccel; Plasmax; ***UK:*** Haemaccel.

Protein C

Autoprothrombin IIA; Factor XIV; Proteína C.

ATC — B01AD12.

ATC Vet — QB01AD12.

Drotrecogin Alfa (Activated) *(BAN, rINN)*

Drotrecogina alfa (activada); Drotrécogine Alfa (activé); Drotrecoginum Alfa; Drotrecoginum Alfa (activatum); Drotrekogiini-alfa; Drotrekogin Alfa; LY-203638.

Дротрекогин Альфа (activated)

CAS — 98530-76-8.
ATC — B01AD10.
ATC Vet — QB01AD10.

Incompatibility. In a simulated Y-site study,[1] only 6 of 34 drugs were found to be both physically and chemically compatible with drotrecogin alfa (activated); these were ceftriaxone, cisatracurium, fluconazole, glyceryl trinitrate, potassium chloride, and vasopressin. Drugs found to be incompatible were adrenaline hydrochloride, albumin, amiodarone hydrochloride, ampicillin with sulbactam, ceftazidime, ciclosporin, ciprofloxacin, clindamycin, dobutamine hydrochloride, dopamine hydrochloride, fosphenytoin, furosemide, gentamicin sulfate, heparin sodium, imipenem with cilastatin, insulin, levofloxacin, magnesium sulfate, metronidazole, midazolam hydrochloride, nitroprusside sodium, noradrenaline acid tartrate, piperacillin with tazobactam, potassium phosphate, ranitidine hydrochloride, ticarcillin with clavulanic acid, tobramycin sulfate, and vancomycin hydrochloride.

1. Mann HJ, *et al.* Physical and chemical compatibility of drotrecogin alfa (activated) with 34 drugs during simulated Y-site administration. *Am J Health-Syst Pharm* 2004; **61:** 2664–71. Correction. *ibid.* 2005; **62:** 1134.

Adverse Effects and Precautions

As with other plasma-derived products, protein C preparations carry a risk of transmission of infection. Hypersensitivity reactions have been reported infrequently. Antibodies to protein C may develop in patients treated for congenital protein C deficiency.

Drotrecogin alfa (activated) may increase the risk of severe bleeding episodes. When used in patients with severe sepsis, it is therefore contra-indicated in those who are at low risk for death, such as those with single-organ failure, especially after surgery. It is also contra-indicated in patients with active internal bleeding and in those in which bleeding could be associated with a high risk of death or significant morbidity. Drotrecogin alfa (activated) should be used with caution when there is any other increased risk of bleeding. Drotrecogin alfa (activated) should be stopped 2 hours before any invasive surgery or procedure with an inherent risk of bleeding; it may be restarted 12 hours after major invasive procedures or surgery, or immediately after uncomplicated less invasive procedures, if adequate haemostasis has been achieved.

Effects on the blood. The safety data from early clinical studies and spontaneous reports during clinical use of drotrecogin alfa (activated) have been reviewed.[1] The overall rate of serious bleeding events was 5.3% during the 28-day study period. Serious bleeding events that were considered to be probably related to the use of drotrecogin alfa (activated) occurred in between 2.1% and 2.8% of patients, and often during the infusion period. Risks associated with serious bleeding events were invasive procedures and severe thrombocytopenia; meningitis may also be a risk factor for intracranial haemorrhage. It was recommended that drotrecogin alfa (activated) should not be used when the platelet count is less than 30 000/mm^3.

A subsequent large, multicentre randomised study in patients with severe sepsis, but a low risk of death (the ADDRESS study), confirmed the increased incidence of bleeding in patients with single organ failure who had undergone recent surgery (within 30 days); these patients also had an increased death rate (see Severe Sepsis, below).

1. Bernard GR, *et al.* Safety assessment of drotrecogin alfa (activated) in the treatment of adult patients with severe sepsis. *Crit Care* 2003; **7:** 155–63.

Interactions

When oral anticoagulants such as warfarin are started in patients receiving protein C replacement therapy, a transient hypercoagulable state may occur because of the rapid suppression of vitamin K-dependent protein C activity. An initial low dose of the oral anticoagulant should be increased gradually, and protein C replacement continued, until anticoagulation is stabilised. The risk of bleeding may be increased if tissue plasminogen activator and protein C are used together.

The risk of bleeding with drotrecogin alfa (activated) may be increased if it is used with other drugs that affect haemostasis, such as thrombolytics, oral anticoagulants, antiplatelet drugs, glycoprotein IIb/IIIa-receptor antagonists, and prostacyclins. Low doses of heparin for venous thromboembolism prophylaxis may be used with drotrecogin alfa (activated) without increased risk of serious bleeding. However, in a study of patients with severe sepsis who were already receiving prophylactic heparin, the risks of death and serious adverse events were increased if heparin was stopped when drotrecogin alfa (activated) was started; the reason for this was unclear.

Pharmacokinetics

During continuous infusion for the management of severe sepsis, steady-state plasma concentrations of drotrecogin alfa (activated) are reached in about 2 hours. It is inactivated by plasma protease inhibitors and rapidly cleared from the circulation, falling to below measurable limits within about 2 hours of stopping the infusion.

◊ References.

1. Macias WL, *et al.* Pharmacokinetic-pharmacodynamic analysis of drotrecogin alfa (activated) in patients with severe sepsis. *Clin Pharmacol Ther* 2002; **72:** 391–402.
2. Levy H, *et al.* Obesity does not alter the pharmacokinetics of drotrecogin alfa (activated) in severe sepsis. *Ann Pharmacother* 2005; **39:** 262–7.

Uses and Administration

Protein C is an endogenous inhibitor of blood coagulation (see Haemostasis and Fibrinolysis, p.1045). A preparation of protein C purified from human plasma is used in the management of thromboembolic disorders in patients with congenital deficiency of protein C. The dose should be adjusted according to response in protein C activity. Licensed UK product information suggests an initial dose of 60 to 80 international units/kg. In the USA, an initial dose of 100 to 120 international units/kg is suggested for acute episodes and short-term prophylaxis of thromboembolism, followed by 3 doses of 60 to 80 units/kg every 6 hours, then maintenance doses of 45 to 60 units/kg every 6 or 12 hours. Doses of 45 to 60 units/kg every 12 hours are suggested for long-term prophylaxis. As a solution of 100 international units/mL it is given by intravenous injection at a maximum rate of 2 mL/minute.

Drotrecogin alfa (activated) is a recombinant activated protein C that is used in the management of severe sepsis in high-risk patients with multiple organ failure. It is given by intravenous infusion in a dose of 24 micrograms/kg per hour for 96 hours. Treatment should be started within 48 hours, and preferably within 24 hours, of the onset of sepsis-induced organ dysfunction.

For the use of protein C and drotrecogin alfa (activated) in children, see below.

Administration in children. Dosage regimens of protein C used for children and neonates with protein C deficiency are the same as those used in adults (see above). However, for children weighing less than 10 kg the rate of injection should not exceed 0.2 mL/kg per minute.

Drotrecogin alfa (activated) is not licensed for use in children under 18 years of age (see also Severe Sepsis, below).

Severe sepsis. Severe sepsis (sepsis associated with acute organ dysfunction; see Septicaemia, p.190) involves a systemic inflammatory response, inappropriate coagulation, and impaired fibrinolysis. These contribute to the development of disseminated intravascular coagulation (DIC) and microvascular thrombosis (p.1048). Endogenous protein C becomes depleted as it is activated in an attempt to restore homoeostasis. In the small number of cases that have been reported,[1-3] protein C replacement appeared to improve rate of survival and clinical outcome in the management of purpura fulminans and DIC in severe meningococcaemia. Protein C has also been used in a few patients with purpura fulminans associated with sepsis caused by other organisms such as *Streptococcus pneumoniae*.[4]

Drotrecogin alfa (activated) has been studied in the management of severe sepsis and found to reduce morbidity and mortality, but with an increased risk of serious bleeding events[5-9] (see also Effects on the Blood, above). Pooled study data suggested that earlier treatment (within 24 hours of first organ dysfunction) was associated with more benefit than later treatment,[10] and subgroup analysis suggested that the benefits were greatest in those at greater risk of death.[11] A subsequent large, multicentre randomised study[12] (the ADDRESS trial) examined the effects of drotrecogin alfa (activated) in patients with severe sepsis but a low risk of death (APACHE II score less than 25, or single organ failure). The study was terminated early, as interim analysis indicated that there was no benefit from active therapy, and in the subgroup of patients with single organ failure who had undergone surgery within the last 30 days, those given the drug appeared to have a higher mortality rate than those assigned to placebo. Various regulatory bodies have issued guidance restricting the use of drotrecogin alfa (activated) to high-risk patients under specialist care.[13-15]

Similar results to those in adults have been reported in initial studies of drotrecogin alfa (activated) in children.[16,17] However, a large placebo-controlled study was stopped early when an interim analysis found that drotrecogin alfa (activated) was highly unlikely to show an improvement over placebo in the primary end-point of composite time to complete organ failure resolution over 14 days.[18] The analysis also found an increase in the rate of CNS bleeding in the drotrecogin alfa (activated) group. The efficacy of drotrecogin alfa (activated) does not appear to depend on the identity of the infective organism.[19]

1. Rintala E, *et al.* Protein C in the treatment of coagulopathy in meningococcal disease. *Lancet* 1996; **347:** 1767.
2. Smith OP, *et al.* Use of protein-C concentrate, heparin, and haemodiafiltration in meningococcus-induced purpura fulminans. *Lancet* 1997; **350:** 1590–3.
3. Alberio L, *et al.* Protein C replacement in severe meningococcemia: rationale and clinical experience. *Clin Infect Dis* 2001; **32:** 1338–46. Correction. *ibid.*; 1803.
4. Rintala E, *et al.* Protein C substitution in sepsis-associated purpura fulminans. *Crit Care Med* 2000; **28:** 2373–8.
5. Bernard GR, *et al.* The Recombinant Human Activated Protein C Worldwide Evaluation in Severe Sepsis (PROWESS) Study Group. Efficacy and safety of recombinant human activated protein C for severe sepsis. *N Engl J Med* 2001; **344:** 699–709.
6. Lyseng-Williamson KA, Perry CM. Drotrecogin alfa (activated). *Drugs* 2002; **62:** 617–30.
7. Vincent J-L, *et al.* Effects of drotrecogin alfa (activated) on organ dysfunction in the PROWESS trial. *Crit Care Med* 2003; **31:** 834–40.
8. Bernard GR, *et al.* Extended evaluation of recombinant human activated protein C United States Trial (ENHANCE US): a single-arm, phase 3B, multicenter study of drotrecogin alfa (activated) in severe sepsis. *Chest* 2004; **125:** 2206–16.
9. Vincent J-L, *et al.* Drotrecogin alfa (activated) treatment in severe sepsis from the global open-label trial ENHANCE: further evidence for survival and safety and implications for early treatment. *Crit Care Med* 2005; **33:** 2266–77.
10. Vincent J-L, *et al.* Use of an integrated clinical trial database to evaluate the effect of timing of drotrecogin alfa (activated) treatment in severe sepsis. *Crit Care* 2006; **10:** R74.
11. Ely EW, *et al.* Drotrecogin alfa (activated) administration across clinically important subgroups of patients with severe sepsis. *Crit Care Med* 2003; **31:** 12–19.
12. Abraham E, *et al.* Drotrecogin alfa (activated) for adults with severe sepsis and a low risk of death. *N Engl J Med* 2005; **353:** 1332–41.
13. NICE. Drotrecogin alfa (activated) for severe sepsis: Technology Appraisal 84 (September 2004). Available at: http://www.nice.org.uk/nicemedia/pdf/TA084guidance.pdf (accessed 01/09/08)
14. European Medicines Agency (EMEA) Committee for Medicinal Products for Human Use. Press release (issued 21st April 2005). Available at: http://www.emea.europa.eu/pdfs/human/press/pr/13844405en.pdf (accessed 01/09/08)
15. Commission on Human Medicines/Medicines and Healthcare products Regulatory Agency. Drotrecogin alfa (activated) (Xigris): risk-benefit in the management of sepsis. *Current Problems* 2006; **31:** 3. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2023860&RevisionSelectionMethod=LatestReleased (accessed 23/05/07)
16. Barton P, *et al.* Safety, pharmacokinetics, and pharmacodynamics of drotrecogin alfa (activated) in children with severe sepsis. *Pediatrics* 2004; **113:** 7–17.
17. Goldstein B, *et al.* ENHANCE: results of a global open-label trial of drotrecogin alfa (activated) in children with severe sepsis. *Pediatr Crit Care Med* 2006; **7:** 200–211.
18. Nadel S, *et al.* REsearching severe Sepsis and Organ dysfunction in children: a gLobal perspective (RESOLVE) study group. Drotrecogin alfa (activated) in children with severe sepsis: a multicentre phase III randomised controlled trial. *Lancet* 2007; **369:** 836–43.
19. Opal SM, *et al.* Systemic host responses in severe sepsis analyzed by causative microorganism and treatment effects of drotrecogin alfa (activated). *Clin Infect Dis* 2003; **37:** 50–8.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Xigris; ***Austral.:*** Xigris; ***Austria:*** Ceprotin; Xigris; ***Belg.:*** Ceprotin; Xigris; ***Braz.:*** Xigris; ***Canad.:*** Xigris; ***Chile:*** Xigris; ***Cz.:*** Ceprotin; Xigris; ***Denm.:*** Ceprotin; Xigris; ***Fin.:*** Ceprotin; Xigris; ***Fr.:*** Ceprotin; Protexel; Xigris; ***Ger.:*** Ceprotin; Xigris; ***Gr.:*** Ceprotin; Xigris; ***Hong Kong:*** Xigris; ***Hung.:*** Xigris; ***India:*** Xigris; ***Irl.:*** Xigris; ***Israel:*** Xigris; ***Ital.:*** Ceprotin; Xigris; ***Malaysia:*** Xigris; ***Mex.:*** Xigris; ***Neth.:*** Ceprotin; Xigris; ***Norw.:*** Ceprotin; Xigris; ***NZ:*** Xigris; ***Pol.:*** Ceprotin; Xigris; ***Port.:*** Ceprotin; Xigris; ***Rus.:*** Xigris (Экигрис); ***S.Afr.:*** Xigris; ***Singapore:*** Xigris; ***Spain:*** Ceprotin; Xigris; ***Swed.:*** Ceprotin; Xigris; ***Switz.:*** Ceprotin; Xigris; ***Turk.:*** Xigris; ***UK:*** Ceprotin; Xigris; ***USA:*** Ceprotin; Xigris; ***Venez.:*** Xigris.

Red Blood Cells ⊗

Eritrocitos.

Pharmacopoeias. Many pharmacopoeias have monographs, including *US*.

USP 31 (Red Blood Cells). It is the portion of blood that contains haemoglobin and is derived from human whole blood (from which plasma and platelets are removed by centrifugation, sedimentation) or by apheresis. Red blood cells may be further processed by addition of red cell preservatives, irradiation to inactivate lymphocytes, filtration for removal of leucocytes, washing