Thrombocytopenia. References.

1. Tepler I, *et al.* A randomized placebo-controlled trial of recombinant human interleukin-11 in cancer patients with severe thrombocytopenia due to chemotherapy. *Blood* 1996; **87:** 3607–14.
2. Isaacs C, *et al.* Randomized placebo-controlled study of recombinant human interleukin-11 to prevent chemotherapy-induced thrombocytopenia in patients with breast cancer receiving dose-intensive cyclophosphamide and doxorubicin. *J Clin Oncol* 1997; **15:** 3368–77.
3. Reynolds CH. Clinical efficacy of rhIL-11. *Oncology (Huntingt)* 2000; **14** (suppl 8): 32–40.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Neumega†; ***Braz.:*** Neumega; ***Chile:*** Neumega†; ***Mex.:*** Neumega†; ***USA:*** Neumega; ***Venez.:*** Neumega.

Oxidised Cellulose

Cellulosic Acid; Celulosa oxidada; Oxidized Cellulose.

CAS — 9032-53-5.
ATC — B02BC02.
ATC Vet — QB02BC02.

Description. Oxidised cellulose is a sterile polyanhydroglucuronic acid, prepared by the oxidation of a suitable form of cellulose.

Pharmacopoeias. In *US* which also includes Oxidized Regenerated Cellulose.
USP 31 (Oxidized Cellulose). It contains not less than 16% and not more than 24% of carboxyl groups, calculated on the dried basis. It is a slightly off-white gauze or lint with a slight, charred odour. Insoluble in water and in acids; soluble in dilute alkalis. Store at a temperature not exceeding 8°. Protect from direct sunlight.
USP 31 (Oxidized Regenerated Cellulose). It contains 18 to 24% of carboxyl groups calculated on the dried basis. It is a slightly off-white knit fabric, with a slight odour. Insoluble in water and in dilute acids; soluble in dilute alkalis. Store at a temperature between 15° and 30°. Protect from direct sunlight.

Adverse Effects and Precautions

Foreign body reactions may occur after the use of oxidised cellulose or oxidised regenerated cellulose. Headache, burning, and stinging have been reported and sneezing has been noted after use in epistaxis. Oxidised cellulose swells on contact with a bleeding surface; this could result in tissue necrosis, nerve damage, obstruction, or vascular stenosis if packed closely, especially into bony cavities, or if wrapped tightly around blood vessels. To minimise such complications the removal of excess material should be considered after haemostasis is achieved, and oxidised cellulose should always be removed after use near the spinal cord or optic nerve. Oxidised cellulose should not be used in packing or implantation for fractures since it may interfere with bone regeneration or cause cyst formation. It should not be used as a surface dressing, except for immediate control of haemorrhage, as it inhibits epithelialisation.

Oxidised cellulose should be used as the dry material since moistening will reduce its ability to absorb blood. Silver nitrate or other escharotic chemicals should not be applied before use as cauterisation might inhibit absorption of oxidised cellulose. Thrombin is inactivated by the low pH of oxidised cellulose; it is recommended that oxidised cellulose should not be impregnated with other haemostatics or antibacterials.

Uses and Administration

Oxidised cellulose and oxidised regenerated cellulose are absorbable haemostatics (p.1045). When applied to a bleeding surface, they swell to form a gelatinous mass which aids in the formation of a clot. It is gradually absorbed by the tissues, usually within 7 to 14 days. These materials also have a weak bactericidal action. They are used in surgery as adjuncts in the control of moderate bleeding where suturing or ligation is impracticable or ineffective; they should not be used to control haemorrhage from large arteries. The gauze, lint, or knitted material should be laid on the bleeding surface or held firmly against the tissues until haemostasis is achieved; removal should then be considered (see Adverse Effects and Precautions, above). Oxidised cellulose should be used as the dry material as moistening will reduce its ability to absorb blood.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Surgicel; ***Ger.:*** Tabotamp; ***Hong Kong:*** Seal On†; ***Irl.:*** Alltracel P†; Premdoc†; Seal-On; Traumacel P; ***Ital.:*** Tabotamp; ***UK:*** Oxycel; StopBleed; ***USA:*** Oxycel; Surgicel.

Multi-ingredient: ***Fr.:*** Promogran; ***Irl.:*** Alltracel S†; ***Ital.:*** Promogran; ***UK:*** Seal-On.

Oxypolygelatin ⊗

Oxipoligelatina.

Profile

Oxypolygelatin is a polymer derived from gelatin (p.1072). It is used as a 5.5% solution as a plasma volume expander. There have been reports of anaphylaxis.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Gelifundol†; ***Austria:*** Gelifundol; ***Cz.:*** Gelifundol†; ***Ger.:*** Gelifundol†; ***Hong Kong:*** Gelifundol†; ***Hung.:*** Gelifundol†; ***S.Afr.:*** Gelifundol†; ***Thai.:*** Gelifundol.

Pegzerepoetin Alfa ⊗

Methoxy Polyethylene Glycol-Epoetin Beta; Pegserepoetin Alfa; R-744; Ro-50-3821. 1-165-Erythropoietin (human) monoamide with α-(3-carboxypropyl)-ω-methoxypoly(oxy-1,2-ethanediyl).

CAS — 677324-53-7.
ATC — B03XA03.
ATC Vet — QB03XA03.

Adverse Effects and Precautions

As for Epoetins, p.1061.

Pharmacokinetics

In patients with chronic renal impairment, pegzerepoetin alfa is absorbed after subcutaneous injection with an absolute bioavailability of about 60%. It has a terminal elimination half-life of about 134 hours after intravenous injection and about 140 hours when given subcutaneously. Haemodialysis does not affect the pharmacokinetics of pegzerepoetin alfa.

Uses and Administration

Pegzerepoetin alfa is described as a continuous erythropoietin receptor activator (CERA). It has similar properties to the epoetins (p.1062), but a longer duration of action. Pegzerepoetin alfa is used in the treatment of anaemia associated with chronic renal failure (see Normocytic-normochromic Anaemia, p.1044). A starting dose of 600 nanograms/kg is given once every 2 weeks as a single intravenous or subcutaneous injection. The dose may be adjusted by about 25%, at monthly intervals, so that the rate of rise of haemoglobin is between 1 and 2 g per 100 mL each month. When the target haemoglobin concentration of between 11 and 12 g per 100 mL has been achieved, a maintenance dose of pegzerepoetin alfa may be given once monthly; this is equal to twice the dose that had been given once every 2 weeks.

Pegzerepoetin alfa is also under investigation in the treatment of anaemia in patients with non-myeloid malignant disease receiving chemotherapy.

◊ References.

1. de Francisco ALM, *et al.* BA16260 Study Investigators. Continuous Erythropoietin Receptor Activator (C.E.R.A.) administered at extended administration intervals corrects anaemia in patients with chronic kidney disease on dialysis: a randomised, multicentre, multiple-dose, phase II study. *Int J Clin Pract* 2006; **60:** 1687–96.
2. Sulowicz W, *et al.* PROTOS Study Investigators. Once-monthly subcutaneous C.E.R.A. maintains stable hemoglobin control in patients with chronic kidney disease on dialysis and converted directly from epoetin one to three times weekly. *Clin J Am Soc Nephrol* 2007; **2:** 637–46.
3. Levin NW, *et al.* MAXIMA study investigators. Intravenous methoxy polyethylene glycol-epoetin beta for haemoglobin control in patients with chronic kidney disease who are on dialysis: a randomised non-inferiority trial (MAXIMA). *Lancet* 2007; **370:** 1415–21.
4. Österborg A, *et al.* Phase II study of three dose levels of continuous erythropoietin receptor activator (C.E.R.A.) in anaemic patients with aggressive non-Hodgkin's lymphoma receiving combination chemotherapy. *Br J Haematol* 2007; **136:** 736–44.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Mircera; ***Fr.:*** Mircera; ***Port.:*** Mircera; ***UK:*** Mircera; ***USA:*** Mircera.

Plasma

Pharmacopoeias. Many pharmacopoeias have monographs, including *Eur.* (see p.vii).
Ph. Eur. 6.2 (Human Plasma for Fractionation; Plasma Humanum ad Separationem). The liquid part of human blood remaining after separation of the cellular elements from whole blood or collected in an apheresis procedure; it is intended for the manufacture of plasma-derived products. It is obtained from healthy donors and is tested for the absence of hepatitis B surface antigen and antibodies against HIV-1 and HIV-2 and hepatitis C virus.
A light yellow to green, clear or slightly turbid liquid, without visible signs of haemolysis. Frozen plasma should be stored at or below –20°; it may still be used for fractionation if the temperature is between –20° and –15° for not more than a total of 72 hours without exceeding –15° on more than one occasion as long as the temperature is at all times –5° or lower.
Ph. Eur. 6.2 (Human Plasma (Pooled and Treated for Virus Inactivation); Plasma Humanum Coagumentum Conditumque ad Exstinguendum Virum). A frozen or freeze-dried, sterile, non-pyrogenic preparation obtained from human plasma derived from donors belonging to the same ABO blood group. The plasma used complies with the requirements for Human Plasma for Fractionation (above). The method of preparation is designed to minimise activation of any coagulation factor and includes a step or steps that have been shown to inactivate known agents of infection.
The frozen preparation, after thawing, is a clear or slightly opalescent liquid free from solid and gelatinous particles. The freeze-dried preparation is an almost white or slightly yellow powder or friable solid.

Adverse Effects and Precautions

As for Blood, p.1056, though with a low risk of transmitting cell-associated viruses. However, the production of blood products using plasma from UK donors has been phased out due to the possible risk of transmission of Creutzfeldt-Jakob disease.

Uses and Administration

Fresh frozen plasma contains useful amounts of clotting factors. It should be reserved for patients with proven abnormalities in blood coagulation. Indications include congenital deficiencies in clotting factors for which specific concentrates are unavailable, severe multiple clotting factor deficiencies (for example in patients with liver disease), rapid reversal of the action of coumarin anticoagulants, and disseminated intravascular coagulation. It may be used after massive blood transfusion when there is evidence of coagulation deficiency but its value for routine prophylaxis against abnormal bleeding tendencies in patients receiving massive blood transfusions is contentious except where clotting abnormalities have been confirmed. It has also been used in the treatment of thrombotic thrombocytopenic purpura and as a source of plasma proteins.

The amount of fresh frozen plasma transfused depends on the required level of clotting factors. A unit of fresh frozen plasma refers to the quantity of plasma obtained from 1 unit of whole blood; this generally represents a volume of about 250 mL, including anticoagulant.

Fresh frozen plasma should not be used as a volume expander or as a nutritional source.

Therapeutic plasma exchange or plasmapheresis (see below) are used in a wide variety of disorders.

Plasma is used to prepare blood products including albumin, antithrombin III, blood clotting factors, immunoglobulins, and platelets. Other preparations include cryoprecipitate depleted plasma, which is deficient in fibrinogen, factor VIII, von Willebrand factor, cryoglobulin, and fibronectin, and single donor plasma, which is not frozen. A solvent-detergent-treated plasma preparation is available.

Guidelines and reviews. General references to the use of plasma.

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. Cohen H, *et al.* Plasma, plasma products, and indications for their use. In: Contreras M, ed. *ABC of transfusion*. 3rd ed. London; BMJ Books, 1998: 40–44.
3. British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. *Br J Haematol* 2004; **126:** 11–28. Also available at: http://www.bcshguidelines.com/pdf/freshfrozen_280604.pdf (accessed 27/10/05) Addenda, amendments, and corrections (4 sets) at http://www.bcshguidelines.com/pdf/Amendments_FFP_091205.pdf (issued 07/12/05), *ibid.* 2007; **136:** 514–16, at http://www.bcshguidelines.com/pdf/FFPAmendment_1_17_Oct_2007.pdf (issued 17/10/07), at http://www.bcshguidelines.com/pdf/FFPAmendment_2_17_Oct_2007.pdf (issued 17/10/07) (accessed 19/06/08)
4. Stanworth SJ, *et al.* Is fresh frozen plasma clinically effective? A systematic review of randomized controlled trials. *Br J Haematol* 2004; **126:** 139–52.