to remove proteins, freezing and thawing, or rejuvenation using validated and approved procedures.

For preparations derived from whole blood, one unit (dose) of Red Blood Cells contains a minimum of 50 g of haemoglobin. One unit of Red Blood Cells, Leukocytes Reduced contains a minimum of 42.5 g of haemoglobin and has a residual leucocyte count of less than 5×10^6. One unit of Red Blood Cells, Deglycerolized contains a minimum of 40 g of haemoglobin. One unit of Red Blood Cells, Leukocytes Reduced and Deglycerolized contains a minimum of 34 g of haemoglobin and has a residual leucocyte count of less than 5×10^6.

For preparations derived by apheresis, one unit (dose) of Red Blood Cells, Pheresis contains a mean haemoglobin content of 60 g of haemoglobin. One unit of Red Blood Cells, Pheresis, Leukocytes Reduced contains a mean haemoglobin content of 51 g of haemoglobin and has a residual leucocyte count of less than 5×10^6.

Red blood cells should be stored in the original container, or transferred to an equivalent container using a technique that does not compromise sterility. An approved additive solution may be added after removal of the plasma. Liquid red blood cells is stored at 1° to 6°. Frozen red blood cells is stored at or below –65°.

Red blood cells in Anticoagulant Citrate Dextrose Solution, Anticoagulant Citrate Phosphate Dextrose Solution, or in Anticoagulant Citrate Phosphate Dextrose-Dextrose Solution may be stored for up to 21 days at 1° to 6° after the blood has been drawn. Red blood cells in Anticoagulant Citrate Dextrose Phosphate Adenine Solution may be stored for up to 35 days at 1° to 6°. Red blood cells may be stored in an approved additive solution for up to 42 days at 1° to 6°.

Frozen red blood cells prepared with low glycerol content (20%) may be stored at or below –120° for not later than 10 years from years from the date of collection. Frozen red blood cells prepared with high glycerol content (40%) may be stored at or below –65° for not later than 10 years from years from the date of collection. If the frozen red blood cells is processed for freezing or for thawing, in an open system, the expiry date for the thawed red blood cells is 24 hours after removal from –65° storage, provided it is then stored at the temperature of unfrozen red blood cells.

Dark red in colour when packed and may show a slight creamy layer on the surface and a small supernatant layer of yellow or opalescent plasma.

Adverse Effects and Precautions

As for Blood, p.1056.

Antibody formation. Patients with sickle-cell anaemia frequently require repeated transfusions of red blood cells. Alloimmunisation is a common problem in these patients, and has the potential to cause haemolytic transfusion reactions.[1] Alloantibodies were detected in 32 of 107 black patients with sickle-cell anaemia who had received red cell transfusions compared with 1 of 19 non-black patients who had received transfusions for other chronic anaemias.[2] The incidence of antibody formation was related to the number of transfusions received. An analysis of the red cell phenotypes suggested that the high rate of alloimmunisation among patients with sickle-cell anaemia could be due to racial differences between donors and recipients. Alloimmunisation can also occur in thalassaemia patients who are given transfusions,[3] and the incidence in these patients may also be affected by racial differences between donors and recipients.[4] Erythrocyte autoantibody formation has also been reported.[1,3]

1. Aygun B, *et al.* Clinical significance of RBC alloantibodies and autoantibodies in sickle cell patients who received transfusions. *Transfusion* 2002; **42:** 37–43.
2. Vichinsky EP, *et al.* Alloimmunization in sickle cell anemia and transfusion of racially unmatched blood. *N Engl J Med* 1990; **322:** 1617–21.
3. Singer ST, *et al.* Alloimmunization and erythrocyte autoimmunization in transfusion-dependent thalassemia patients of predominantly Asian descent. *Blood* 2000; **96:** 3369–73.
4. Ho H-K, *et al.* Alloimmunization in Hong Kong southern Chinese transfusion-dependent thalassemia patients. *Blood* 2001; **97:** 3999–4000.

Uses and Administration

Transfusions of red blood cells are given for the treatment of severe anaemia without hypovolaemia (p.1042).

Red blood cells are also used for exchange transfusion in babies with haemolytic disease of the newborn (p.2204). Red cells may be used with volume expanders for acute blood loss of less than half of the blood volume; if more than half of the blood volume has been lost, whole blood should be used.

Other red blood cell products are available. Concentrated red cells in an optimal additive solution containing sodium chloride, adenine, glucose, and mannitol has reduced viscosity and an extended shelf-life. Leucocyte-depleted red cells may be used in patients who have developed antibodies to previous transfusions or in whom development of antibodies is undesirable. Frozen, thawed, and washed red cell concentrates in which plasma proteins are removed in addition to leucocytes and platelets may be used in patients with rare antibodies.

◊ Reviews and guidelines.

1. Davies SC, Williamson LM. Transfusion of red cells. In: Contreras M, ed. *ABC of transfusion*. 3rd ed. London: BMJ Books, 1998: 10–16.
2. 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)
3. British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the clinical use of red cell transfusions. *Br J Haematol* 2001; **113:** 24–31. Also available at: http://www.bcshguidelines.com/pdf/bjh2701.pdf (accessed 27/10/05)
4. Hill SR, *et al.* Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2000 (accessed 16/06/05).

Preparations

USP 31: Red Blood Cells.

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** Vulnofilin Compuesto†.

Romiplostim *(USAN, rINN)*

AMG-531; Romiplostimum. L-Methionyl[human immunoglobulin heavy constant gamma 1-(227 *C*-terminal residues)-peptide (Fc fragment)] fusion protein with 41 amino acids peptide, (7-7′:10,10′)-bisdisulfide dimer.

Ромиплостим

CAS — 267639-76-9.

Profile

Romiplostim is a protein that acts as an agonist at the thrombopoietin receptor to stimulate platelet production, although it has no sequence homology with endogenous thrombopoietin. It is under investigation in the treatment of chronic idiopathic thrombocytopenic purpura.

◊ References.

1. Bussel JB, *et al.* AMG 531, a thrombopoiesis-stimulating protein, for chronic ITP. *N Engl J Med* 2006; **355:** 1672–81. Correction. *ibid.*; 2054.
2. Kuter DJ, *et al.* Efficacy of romiplostim in patients with chronic immune thrombocytopenic purpura: a double-blind randomised controlled trial. *Lancet* 2008; **371:** 395–403.

Sargramostim *(BAN, USAN, rINN)*

BI-61.012; rhu GM-CSF; Sargramostimum. A recombinant human granulocyte-macrophage colony-stimulating factor; 23-L-Leucinecolony-stimulating factor 2 (human clone pHG_{25} protein moiety).

Сарграмостим

CAS — 123774-72-1.

ATC — L03AA09.

ATC Vet — QL03AA09.

Pharmacopoeias. In *US.*

USP 31 (Sargramostim). A single chain, glycosylated polypeptide of 127 amino acid residues expressed from *Saccharomyces cerevisiae*. The glycoprotein primarily consists of three molecular species having relative molecular weights of about 19 500, 16 800, and 15 500 due to different levels of glycosylation. Sargramostim has the property of generating granulocyte, macrophage, and mixed granulocyte macrophage colonies from haematopoietic progenitor cells found in bone marrow. Store in sealed containers at a temperature of –20° or below.

Stability. Solutions of sargramostim may be adsorbed onto glass or plastic materials and so albumin must be added to give a final concentration of 1 mg/mL to solutions that are diluted to concentrations of sargramostim below 10 micrograms/mL.

Adverse Effects and Precautions

As for Molgramostim, p.1073.

Uses and Administration

Sargramostim is a granulocyte-macrophage colony-stimulating factor with actions and uses similar to those of molgramostim (p.1074). It is used to treat or prevent neutropenia in patients receiving myelosuppressive cancer chemotherapy and to reduce the period of neutropenia in patients undergoing bone marrow transplantation (p.640). It is also used after bone marrow transplantation when engraftment is delayed or has failed. Sargramostim may be used to mobilise peripheral blood progenitor cells for collection and subsequent use in autologous peripheral blood stem cell transplantation, as well as after transplantation to improve engraftment.

As an **adjunct to antineoplastic therapy**, sargramostim is given by intravenous infusion over 4 hours in a dose of 250 micrograms/m^2 daily for up to 42 days as required.

After **bone marrow transplantation**, sargramostim may be given in a dose of 250 micrograms/m^2 daily by intravenous infusion over 2 hours. When engraftment is delayed or has failed, a course of sargramostim 250 micrograms/m^2 daily for 14 days may be used. The dose can be repeated after a 7-day interval if engraftment has not occurred. A third course of 500 micrograms/m^2 daily for 14 days may be tried after another 7-day interval if needed, but further dose escalation is unlikely to be of benefit.

For **mobilisation** of peripheral blood progenitor cells a dose of 250 micrograms/m^2 daily is given by continuous intravenous infusion over 24 hours or by subcutaneous injection, with leucapheresis usually starting on day 5. The same dosing regimen may be used after peripheral blood stem cell transplantation, until neutrophil recovery.

HIV infection and AIDS. Sargramostim has been evaluated in the management of HIV infection (p.856). There is some evidence to suggest that it might help to decrease and suppress viral load, and increase CD4+ cell counts, by enhancing the activity of antiretroviral drugs and increasing the resistance of monocytes to HIV infection.[1-3] However, in a study[4] of patients who were medically stable but had incompletely controlled HIV replication, sargramostim did not have a significant antiviral effect and there was only a trend towards increased CD4+ counts. The effect of molgramostim has been studied in a small trial[5] in which it was found to blunt viral rebound following interruption of HAART.

1. Skowron G, *et al.* The safety and efficacy of granulocyte-macrophage colony-stimulating factor (sargramostim) added to indinavir- or ritonavir-based antiretroviral therapy: a randomized double-blind, placebo-controlled trial. *J Infect Dis* 1999; **180:** 1064–71.
2. Brites C, *et al.* A randomized, placebo-controlled trial of granulocyte-macrophage colony-stimulating factor and nucleoside analogue therapy in AIDS. *J Infect Dis* 2000; **182:** 1531–5.
3. Angel JB, *et al.* Phase III study of granulocyte-macrophage colony-stimulating factor in advanced HIV disease: effect on infections, CD4 cell counts and HIV suppression. *AIDS* 2000; **14:** 387–95.
4. Jacobson JM, *et al.* Granulocyte-macrophage colony-stimulating factor induces modest increases in plasma human immunodeficiency virus (HIV) type 1 RNA levels and CD4+ lymphocyte counts in patients with uncontrolled HIV infection. *J Infect Dis* 2003; **188:** 1804–14.
5. Fagard C, *et al.* A controlled trial of granulocyte macrophage-colony stimulating factor during interruption of HAART. *AIDS* 2003; **17:** 1487–92.

Inflammatory bowel disease. A small dose-escalating study[1] reported a beneficial effect from the use of sargramostim in Crohn's disease (see Inflammatory Bowel Disease, p.1697). A subsequent larger placebo-controlled study[2] in moderate to severe active disease found that the rate of response to sargramostim was not significantly different from that of placebo. Although disease severity and quality of life improved in the sargramostim group, later unpublished study results were said to be disappointing, and in June 2007 the manufacturer declared that it would not be investigating sargramostim any further in Crohn's disease.

1. Dieckgraefe BK, Korzenik JR. Treatment of active Crohn's disease with recombinant human granulocyte-macrophage colony-stimulating factor. *Lancet* 2002; **360:** 1478–80.
2. Korzenik JR, *et al.* Sargramostim for active Crohn's disease. *N Engl J Med* 2005; **352:** 2193–2201.

Malignant neoplasms. It has been suggested that granulocyte-macrophage colony-stimulating factor may be able to increase antitumour immune activity. Sargramostim, given by nebuliser to stimulate a local response, has been investigated in patients with lung metastases.[1,2]

1. Anderson PM, *et al.* Aerosol granulocyte macrophage-colony stimulating factor: a low toxicity, lung-specific biological therapy in patients with lung metastases. *Clin Cancer Res* 1999; **5:** 2316–23.
2. Rao RD, *et al.* Aerosolized granulocyte macrophage colony-stimulating factor (GM-CSF) therapy in metastatic cancer. *Am J Clin Oncol* 2003; **26:** 493–8.

Wounds and ulcers. See under Molgramostim (p.1074) for mention of the use of sargramostim in the promotion of wound healing.

Preparations

USP 31: Sargramostim for Injection.

Proprietary Preparations (details are given in Part 3)

USA: Leukine.

Thrombin *(rINN)*

Factor IIa; Thrombine; Thrombinum; Trombin; Trombina.

Тромбин

CAS — 9002-04-4.
ATC — B02BC06; B02BD30.
ATC Vet — QB02BC06; QB02BD30.

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

USP 31 (Thrombin). A sterile, freeze-dried powder derived from bovine plasma containing the protein substance prepared from prothrombin through interaction with added thromboplastin in the presence of calcium. It is capable, without the addition of other substances, of causing the clotting of whole blood, plasma, or a solution of fibrinogen. It should be stored at 2° to 8°. Once reconstituted, solutions should be used within a few hours of preparation. The label should state that the prepared solution should not be injected into or otherwise allowed to enter large blood vessels.

A white to greyish, amorphous substance dried from the frozen state.

Thrombin Alfa *(USAN, rINN)*

Human thrombin (recombinant, glycosylated); Thrombine Alfa; Thrombinum Alfa; Trombina Alfa. Human thrombin (recombinant, glycofrom α).

Тромбин Альфа

CAS — 869858-13-9.

Adverse Effects and Precautions

Hypersensitivity reactions, including anaphylaxis, have occurred rarely. Thrombin solutions must not be injected into blood vessels.

Antibody formation. Exposure to thrombin preparations of bovine origin has led to the development of antibodies to bovine thrombin and factor V with cross-reactivity, in some cases, to human factors. The presence of inhibitors to human factors may produce bleeding abnormalities and interfere with clotting measurements. Platelet infusions, fresh frozen plasma, and activated prothrombin complex concentrates have been used in the management of acute haemorrhagic complications, though often with limited success. Treatments that have been tried, in order to reduce the antibody titre, have included corticosteroids, ciclosporin, antineoplastics, intravenous immunoglobulin, and plasmapheresis.[1,2] Despite the availability of preparations containing virus-inactivated human fibrinogen the use of bovine thrombin is reported to be widespread and cases of acquired factor V inhibitor continue to occur.[3]

1. Ortel TL. Clinical and laboratory manifestations of anti-factor V antibodies. *J Lab Clin Med* 1999; **133:** 326–34.
2. Streiff MB, Ness PM. Acquired FV inhibitors: a needless iatrogenic complication of bovine thrombin exposure. *Transfusion* 2002; **42:** 18–26.
3. Kirkeby KM, Aronowitz P. Acquired factor V inhibitor: a common and avoidable complication of topical bovine thrombin application. *Am J Med* 2005; **118:** 805.

Uses and Administration

Thrombin is a protein substance produced *in vivo* from prothrombin that converts soluble fibrinogen into insoluble fibrin thus producing coagulation.

Thrombin of either human or bovine origin is applied topically to control bleeding from capillaries and small venules. It is applied directly to the bleeding surface either as a solution or dry powder. It may also be used with absorbable gelatin sponge during surgical procedures. Thrombin alfa, a recombinant human thrombin, is used similarly.

Thrombin is a component of fibrin glue (p.1069).

General references. Reviews.

1. Lundblad RL, *et al.* A review of the therapeutic uses of thrombin. *Thromb Haemost* 2004; **91:** 851–60.

Pseudoaneurysm. An acute pseudoaneurysm is an arterial rupture, contained by fibromuscular tissue, that communicates with the artery via a narrow neck. Insertion-site femoral pseudoaneurysm can occur as a result of procedures such as cardiac catheterisation and peripheral angiography. It is usually treated with ultrasound-guided compression, but this time-consuming technique causes discomfort for both the patient and the staff carrying out the procedure, and may be of limited success for large pseudoaneurysms and patients receiving anticoagulation. Surgical repair may be required in some patients. As an alternative to pressure or surgery, thrombin has been given by ultrasound-guided percutaneous injection. In reported series,[1-4] complete thrombosis of the pseudoaneurysm sac occurred in more than 90% of patients with one injection of bovine thrombin. Bovine thrombin has also been used when compression has failed,[4,5] and a comparative study[6] in 30 patients found thrombin to be more successful than compression. Human thrombin has also been used successfully.[7] A retrospective review[8] concluded that bovine and human thrombin were equally effective. The successful use of autologous thrombin in a few patients has also been described.[9]

1. La Perna L, *et al.* Ultrasound-guided thrombin injection for the treatment of postcatheterization pseudoaneurysms. *Circulation* 2000; **102:** 2391–5.
2. Mohler ER, *et al.* Therapeutic thrombin injection of pseudoaneurysms: a multicenter experience. *Vasc Med* 2001; **6:** 241–4.
3. Olsen DM, *et al.* A prospective study of ultrasound scan-guided thrombin injection of femoral pseudoaneurysm: a trend toward minimal medication. *J Vasc Surg* 2002; **36:** 779–82.
4. Stone P, *et al.* Iatrogenic pseudoaneurysms: comparison of treatment modalities, including duplex-guided thrombin injection. *W V Med J* 2003; **99:** 230–2.
5. Lönn L, *et al.* Treatment of femoral pseudoaneurysms: percutaneous US-guided thrombin injection versus US-guided compression. *Acta Radiol* 2002; **43:** 396–400.
6. Lönn L, *et al.* Prospective randomized study comparing ultrasound-guided thrombin injection to compression in the treatment of femoral pseudoaneurysms. *J Endovasc Ther* 2004; **11:** 570–6.
7. Maleux G, *et al.* Percutaneous injection of human thrombin to treat iatrogenic femoral pseudoaneurysms: short- and midterm ultrasound follow-up. *Eur Radiol* 2003; **13:** 209–12.
8. Vázquez V, *et al.* Human thrombin for treatment of pseudoaneurysms: comparison of bovine and human thrombin sonogram-guided injection. *Am J Roentg* 2005; **184:** 1665–71.
9. Quarmby JW, *et al.* Autologous thrombin for treatment of pseudoaneurysms. *Lancet* 2002; **359:** 946–7.

Preparations

Ph. Eur.: Fibrin Sealant Kit;
USP 31: Thrombin.

Proprietary Preparations (details are given in Part 3)
Austral.: Thrombostat†; ***Canad.:*** Thrombostat†; ***NZ:*** Thrombostat; ***Pol.:*** Gastrotrombina; ***S.Afr.:*** Tisseel; ***USA:*** Evithrom; Recothrom; Thrombinar; Thrombogen†; Thrombostat.

Multi-ingredient: ***Arg.:*** Beriplast P; Tissucol; Tissucol Duo Quick†; ***Austral.:*** Tisseel Duo; ***Austria:*** Beriplast; TachoComb; TachoSil; Tissucol; Tissucol Duo Quick; ***Belg.:*** Tissucol Duo; ***Braz.:*** Beriplast P; Tissucol†; ***Canad.:*** Tisseel; ***Chile:*** Beriplast P; ***Cz.:*** TachoComb†; TachoSil; Tissucol; ***Denm.:*** TachoSil; Tisseel Duo Quick; ***Fin.:*** TachoSil; Tisseel Duo Quick; ***Fr.:*** Beriplast; Quixil; TachoSil; Tissucol; ***Ger.:*** Beriplast; Quixil; TachoComb†; TachoSil; Tissucol Duo S; Tissucol-Kit; ***Gr.:*** Beriplast P; ***Hong Kong:*** Beriplast P; TachoComb; Tisseel; ***Hung.:*** Beriplast P; TachoComb†; Tissucol-Kit; ***Indon.:*** Beriplast; ***Israel:*** Beriplast; Quixil; Tisseel; ***Ital.:*** Beriplast; Quixil; TachoSil; Tissucol; ***Mex.:*** Beriplast P; Tissucol†; ***Neth.:*** Beriplast P; Quixil; TachoSil; Tissucol; Tissucol Duo; ***Norw.:*** TachoSil; ***Pol.:*** Beriplast; ***Port.:*** Quixil; TachoSil; Tissucol Duo; ***Rus.:*** TachoComb (ТахоКомб); ***Spain:*** Beriplast P Combi; TachoSil; Tissucol Duo; ***Swed.:*** TachoSil; Tisseel Duo Quick; ***Switz.:*** Beriplast P; TachoSil; Tissucol; Tissucol Duo S; ***Thai.:*** Fibrin Glue†; TachoComb†; ***Turk.:*** Beriplast P; Tisseel VH; ***UK:*** TachoSil; Tisseel; ***USA:*** Artiss.

Thrombomodulin Alfa *(rINN)*

ART-123; Thrombomoduline Alfa; Thrombomodulinum Alfa; Trombomodulina alfa. 1–498-Thrombomodulin (human clone TMP26/TMJ1 protein moiety reduced).

Тромбомодулин Альфа

CAS — 120313-91-9.

Profile

Endogenous thrombomodulin is a transmembrane protein found on the surface of endothelial cells, which acts as a thrombin receptor. Thrombomodulin-bound thrombin activates protein C, which then inactivates clotting factors and so limits coagulation.

Thrombomodulin alfa, a recombinant form of thrombomodulin, is under investigation in the prophylaxis of venous thromboembolism and the treatment of disseminated intravascular coagulation.

◊ References.

1. Kearon C, *et al.* Dose-response study of recombinant human soluble thrombomodulin (ART-123) in the prevention of venous thromboembolism after total hip replacement. *J Thromb Haemost* 2005; **3:** 962–8.
2. Saito H, *et al.* Efficacy and safety of recombinant human soluble thrombomodulin (ART-123) in disseminated intravascular coagulation: results of a phase III, randomized, double-blind clinical trial. *J Thromb Haemost* 2007; **5:** 31–41.

Thromboplastin

Cytozyme; Thrombokinase; Tromboplastina; Tromboplastyna.

Profile

Tissue thromboplastin (tissue factor; factor III) is a membrane glycoprotein that is released from damaged tissue and initiates coagulation. The term thromboplastin may also be applied to other related substances with similar activity. Commercial preparations may contain tissue extracts comprising a variety of such substances.

Preparations of thromboplastin have been used as haemostatics.

A preparation of thromboplastin derived from rabbit brain is used in the determination of the prothrombin time for the control of anticoagulant therapy (for further details see Uses and Administration of Warfarin Sodium, p.1432).

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Clauden.

Multi-ingredient: ***Braz.:*** Claudemor; ***Port.:*** Claudemor†; ***Venez.:*** Claudemor†.

Thrombopoietin

Trombopoyetina.

Profile

Thrombopoietin is a naturally occurring colony-stimulating factor that regulates thrombopoiesis (see Haematopoiesis, p.1042). Recombinant thrombopoietin, and a form of recombinant thrombopoietin conjugated with polyethylene glycol (pegacaristim, PEG-megakaryocyte growth and development factor, PEG-rHuMGDF), are under investigation. They have been studied in the management of thrombocytopenia (p.1051) in patients receiving myelosuppressive or myeloablative chemotherapy, and in patients with myelodysplastic syndrome or HIV-associated thrombocytopenia. There is also some interest in the use of recombinant forms of thrombopoietin in stem cell mobilisation regimens and to increase platelet counts in healthy apheresis donors. However, some results have been disappointing and there are reports of neutralising antibody development.

General references. Studies and reviews.

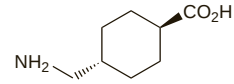
1. Vadhan-Raj S, *et al.* Safety and efficacy of transfusions of autologous cryopreserved platelets derived from recombinant human thrombopoietin to support chemotherapy-associated severe thrombocytopenia: a randomised cross-over study. *Lancet* 2002; **359:** 2145–52.
2. Nomura S, *et al.* Effects of pegylated recombinant human megakaryocyte growth and development factor in patients with idiopathic thrombocytopenic purpura. *Blood* 2002; **100:** 728–30.
3. Schuster MW, *et al.* The effects of pegylated recombinant human megakaryocyte growth and development factor (PEG-rHuMGDF) on platelet recovery in breast cancer patients undergoing autologous bone marrow transplantation. *Exp Hematol* 2002; **30:** 1044–50.
4. Kuter DJ, Begley CG. Recombinant human thrombopoietin: basic biology and evaluation of clinical studies. *Blood* 2002; **100:** 3457–69.
5. Linker C, *et al.* Recombinant human thrombopoietin augments mobilization of peripheral blood progenitor cells for autologous transplantation. *Biol Blood Marrow Transplant* 2003; **9:** 405–13.
6. Vadhan-Raj S, *et al.* Importance of predosing of recombinant human thrombopoietin to reduce chemotherapy-induced early thrombocytopenia. *J Clin Oncol* 2003; **21:** 3158–67.
7. Geissler K, *et al.* Prior and concurrent administration of recombinant human megakaryocyte growth and development factor in patients receiving consolidation chemotherapy for de novo acute myeloid leukemia—a randomized, placebo-controlled, double-blind safety and efficacy study. *Ann Hematol* 2003; **82:** 677–83.

Tranexamic Acid *(BAN, USAN, rINN)*

Acide tranexamique; Ácido tranexámico; Acidum tranexamicum; AMCA; *trans*-AMCHA; CL-65336; Kyselina tranexamová; Traneksaamihappo; Traneksamik Asit; Traneksamo rūgštis; Tranexámsav; Tranexamsyra. *trans*-4-(Aminomethyl)cyclohexanecarboxylic acid.

Транексамовая Кислота

$C_8H_{15}NO_2$ = 157.2.
CAS — 1197-18-8.
ATC — B02AA02.
ATC Vet — QB02AA02.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn.*

Ph. Eur. 6.2 (Tranexamic Acid). A white or almost white, crystalline powder. Freely soluble in water and in glacial acetic acid; practically insoluble in alcohol and in acetone. A 5% solution in water has a pH of 7.0 to 8.0.

Incompatibility. Solutions of tranexamic acid are incompatible with benzylpenicillin.

Adverse Effects

Tranexamic acid appears to be well tolerated. It can produce dose-related gastrointestinal disturbances. Hypotension has occurred, particularly after rapid intravenous dosage. Thrombotic complications have been reported in patients receiving tranexamic acid, but these are usually a consequence of its inappropriate use (see Precautions, below). There have been a few instances of transient disturbance of colour vision associated with use of tranexamic acid; in such cases the drug should be stopped. Hypersensitivity skin reactions have also been reported.

Effects on the eyes. Tranexamic acid has been associated with retinopathy[1] and visual impairment.[2] A haemodialysis patient developed almost total loss of vision within 2 weeks of starting daily tranexamic acid injections after emergency surgery for a bleeding peptic ulcer. Vision was largely restored within a few days of stopping tranexamic acid,[2] although some impairment persisted in conditions of poor light. The patient had experienced visual impairment previously when given tranexamic acid. The authors noted that doses of tranexamic acid should be reduced in patients with renal impairment undergoing dialysis.

A patient undergoing regular peritoneal dialysis for Epstein's syndrome developed ligneous conjunctivitis, gingival hyperpla-