has, however, been some concern raised about the effect of epoetin therapy on patient survival. A placebo-controlled study of epoetin alfa to maintain normal haemoglobin concentrations (12 to 14 g per 100 mL) in patients receiving chemotherapy for metastatic breast cancer was terminated early when an increase in death was found in the epoetin group.[16] In another placebo-controlled study[17] of patients with head and neck cancer undergoing radiotherapy, epoetin beta was associated with correction of anaemia but poorer locoregional progression-free survival. In contrast, analysis of a study[18] in patients with lymphoproliferative malignancies found no effect of epoetin beta on patient survival. Two meta-analyses[14,19] found no conclusive evidence that epoetins affected tumour response or survival, but pointed out that few studies were primarily designed to assess these outcomes. Subsequently, a study of the quality of life in anaemic patients with advanced non-small cell lung cancer was stopped early, when an unplanned safety analysis suggested a reduced overall survival in patients given epoetin alfa.[20] However, two later studies did aim to investigate whether epoetin therapy influenced cancer treatment outcome and survival. One study in women treated with radiochemotherapy for advanced cervical cancer reported no positive correlation between haemoglobin increase and improvement in clinical outcomes, and could not draw a definite conclusion as to whether epoetin beta had an effect on disease progression or survival.[21] Another study, in women given chemotherapy for metastatic breast cancer, found that epoetin beta had no significant effect on overall survival.[22] Nevertheless, a further meta-analysis[23] of studies in cancer patients found that epoetin or darbepoetin alfa therapy was associated with increased risks of venous thromboembolism and death. Studies to date have generally used haemoglobin targets of 12 g and above per 100 mL, and further information is needed on the benefits and risks associated with the lower targets now advised (see Uses and Administration, above). In response to these concerns, authorities have strengthened warnings in licensed product information regarding the use of epoetins and related products in patients with cancer. The MHRA has also advised[24] that blood transfusion should be the preferred option for the management of anaemia in patients with cancer, particularly in those receiving adjuvant chemotherapy or who are being treated with curative intent. They also suggest that transfusion may be preferable in patients with advanced or metastatic cancer who have a good survival prognosis.

Epoetins are sometimes used to treat *anaemias from other causes*. Potential applications include zidovudine-induced anaemia in AIDS patients (see Effects on the Blood under Zidovudine, p.914), postpartum anaemia,[25,26] anaemia in critically ill patients,[27-29] and anaemia of chronic diseases such as rheumatoid arthritis,[30,31] inflammatory bowel disease,[32-34] and chronic heart failure.[35]

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4. Cody J, *et al.* Recombinant human erythropoietin for chronic renal failure anaemia in pre-dialysis patients. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2005 (accessed 27/10/05).
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10. Vamvakas EC, Strauss RG. Meta-analysis of controlled clinical trials studying the efficacy of rHuEPO in reducing blood transfusions in the anemia of prematurity. *Transfusion* 2001; **41:** 406–15.
11. Kotto-Kome AC, *et al.* Effect of beginning recombinant erythropoietin treatment within the first week of life, among very-low-birth-weight neonates, on "early" and "late" erythrocyte transfusions: a meta-analysis. *J Perinatol* 2004; **24:** 24–9.
12. Garcia MG, *et al.* Effect of recombinant erythropoietin on "late" transfusions in the neonatal intensive care unit: a meta-analysis. *J Perinatol* 2002; **22:** 108–11.
13. Dührsen U. The clinical value of erythropoietin in patients with cancer. *Drugs* 2002; **62:** 2013–23.
14. Bohlius J, *et al.* Erythropoietin or darbepoetin for patients with cancer. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2006 (accessed 27/06/08).
15. Jones M, *et al.* Epoetin alfa improves quality of life in patients with cancer: results of a metaanalysis. *Cancer* 2004; **101:** 1720–32.
16. Leyland-Jones B, *et al.* BEST Investigators and Study Group. Maintaining normal hemoglobin levels with epoetin alfa in mainly nonanemic patients with metastatic breast cancer receiving first-line chemotherapy: a survival study. *J Clin Oncol* 2005; **23:** 5960–72.
17. Henke M, *et al.* Erythropoietin to treat head and neck cancer patients with anaemia undergoing radiotherapy: randomised, double-blind, placebo-controlled trial. *Lancet* 2003; **362:** 1255–60.
18. Österborg A, *et al.* Impact of epoetin-β on survival of patients with lymphoproliferative malignancies: long-term follow up of a large randomized study. *Br J Haematol* 2005; **129:** 206–9.
19. Aapro M, *et al.* Effect of treatment with epoetin beta on short-term tumour progression and survival in anaemic patients with cancer: a meta-analysis. *Br J Cancer* 2006; **95:** 1467–73.
20. Wright JR, *et al.* Randomized, double-blind, placebo-controlled trial of erythropoietin in non–small-cell lung cancer with disease-related anemia. *J Clin Oncol* 2007; **25:** 1027–32.
21. Strauss H-G, *et al.* MARCH Investigators and Coordinators. Effects of anemia correction with epoetin beta in patients receiving radiochemotherapy for advanced cervical cancer. *Int J Gynecol Cancer* 2008; **18:** 515–24.
22. Aapro M, *et al.* Effect of once-weekly epoetin beta on survival in patients with metastatic breast cancer receiving anthracycline- and/or taxane-based chemotherapy: results of the Breast Cancer—Anemia and the Value of Erythropoietin (BRAVE) study. *J Clin Oncol* 2008; **26:** 592–8.
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34. Dohil R, *et al.* Recombinant human erythropoietin for treatment of anemia for chronic disease in children with Crohn's disease. *J Pediatr* 1998; **132:** 155–9.
35. Caiola K, Cheng JWM. Use of erythropoietin in heart failure management. *Ann Pharmacother* 2004; **38:** 2145–9.

Cardiovascular diseases. There is some interest in the non-haematopoietic effects of erythropoietin, including protection from apoptosis, antoxidant activity, and pro-angiogenic effects. A possible role in the management of ischaemic stroke and myocardial infarction is under investigation.[1]

1. van der Meer P, *et al.* Erythropoietin in cardiovascular diseases. *Eur Heart J* 2004; **25:** 285–91.

Surgery. Concern over the safety of blood transfusions and the need to conserve blood supplies has led to interest in methods of reducing blood use in surgery. Recombinant human erythropoietin has been used to increase the number of units harvested for autologous transfusion[1] and to reduce transfusion requirements.[2-4] It has also been used as an alternative to blood transfusions in Jehovah's Witnesses.[5-8]

1. Goodnough LT, *et al.* Erythropoietin therapy. *N Engl J Med* 1997; **336:** 933–8.
2. Laupacis A, Fergusson D. Erythropoietin to minimize perioperative blood transfusion: a systematic review of randomized trials. *Transfus Med* 1998; **8:** 309–17.
3. Earnshaw P. Blood conservation in orthopaedic surgery: the role of epoetin alfa. *Int Orthop* 2001; **25:** 273–8.
4. Alghamdi AA, *et al.* Does the use of erythropoietin reduce the risk of exposure to allogeneic blood transfusion in cardiac surgery? A systematic review and meta-analysis. *J Card Surg* 2006; **21:** 320–6.
5. Busuttil D, Copplestone A. Management of blood loss in Jehovah's Witnesses. *BMJ* 1995; **311:** 1115–16.
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7. Hashem B, Dillard TA. A 44-year-old Jehovah's Witness with life-threatening anemia from uterine bleeding. *Chest* 2004; **125:** 1151–4.
8. Holt RL, *et al.* Jehovah's Witnesses requiring complex urgent cardiothoracic surgery. *Ann Thorac Surg* 2004; **78:** 695–7.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Epogen; Eprex; Eritrogen; Hemax; Hypercrit; Pronivel; Recormon; ***Austral.:*** Eprex; NeoRecormon; ***Austria:*** Culat; Erypo; NeoRecormon; Recormon; ***Belg.:*** Eprex; NeoRecormon; ***Braz.:*** Eprex; Eritina; Eritromax; Hemax-Eritron; Hemoprex; Mepotin†; Recormon; Tinax; ***Canad.:*** Eprex; ***Chile:*** Epokine; Eprex; Hypercrit; Recormon; ***Cz.:*** Binocrit; Dynepo; Epomax†; Eprex; NeoRecormon; Recormon†; Retacrit; Silapo; ***Denm.:*** Eprex; NeoRecormon; ***Fin.:*** Eprex; NeoRecormon; ***Fr.:*** Eprex; NeoRecormon; ***Ger.:*** Eprex; Erypo; NeoRecormon; ***Gr.:*** Eprex; NeoRecormon; ***Hong Kong:*** Eprex; Recormon; ***Hung.:*** Eprex; NeoRecormon; ***India:*** Wepox; ***Indon.:*** Epotrex-NP; Eprex; Hemapo; Recormon; ***Irl.:*** Eprex; NeoRecormon; ***Israel:*** Eprex; Recormon; ***Ital.:*** Epoxitin†; Eprex; Globuren†; NeoRecormon; ***Jpn:*** Epogin; Espo; ***Malaysia:*** Eprex; Recormon; ***Mex.:*** Bioyetin; Epomax; Eprex; Erlan; Exetin-A; Hypercrit; Negortire; Recormon; Yepotin; ***Neth.:*** Dynepo; Eprex; NeoRecormon; ***Norw.:*** Eprex; NeoRecormon; ***NZ:*** Eprex; Recormon; ***Philipp.:*** Epokine; Eposino; Eprex; Recormon; Renogen; ***Pol.:*** Eprex; NeoRecormon; ***Port.:*** Dynepo; Eprex; NeoRecormon; Recormon†; Retacrit; Silapo; ***Rus.:*** Epocrin (Эпокрин); Eprex (Эпрекс); Erythrostim (Эритростим); Recormon (Рекормон); ***S.Afr.:*** Eprex; Recormon; Repotin; ***Singapore:*** Eprex; Recormon; ***Spain:*** Epopen; Eprex; NeoRecormon; ***Swed.:*** Eprex; NeoRecormon; ***Switz.:*** Eprex; Recormon; ***Thai.:*** Epokine; Eprex; Espogen; Hemax; Recormon; ***Turk.:*** Eprex; NeoRecormon; ***UAE:*** Epotin; ***UK:*** Binocrit; Dynepo; Eprex; NeoRecormon; Retacrit; ***USA:*** Epogen; Procrit; ***Venez.:*** Eprex; Hypercrit; Recormon.

Etamsylate *(BAN, rINN)*

Cyclonamine; E-141; Etamsilat; Etamsilatas; Etamsilato; Etamsylaatti; Etamsylát; Etamsylat; Étamsylate; Etamsylatum; Etamszilát; Ethamsylate *(USAN)*; MD-141. Diethylammonium 2,5-dihydroxybenzenesulphonate.

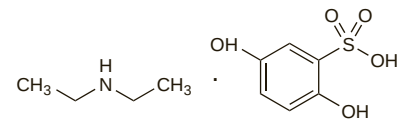
Этамзилат

$C_{10}H_{17}NO_5S$ = 263.3.

CAS — 2624-44-4.

ATC — B02BX01.

ATC Vet — QB02BX01.



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

Ph. Eur. 6.2 (Etamsylate). A white or almost white, crystalline powder. It shows polymorphism. Very soluble in water; soluble in dehydrated alcohol; practically insoluble in dichloromethane; freely soluble in methyl alcohol. A 10% solution in water has a pH of 4.5 to 5.6. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

Nausea, vomiting, diarrhoea, fever, headache, and skin rash have occurred after use of etamsylate. Headache and skin rashes may disappear on reduced dosage, and gastrointestinal disturbances are reduced by giving etamsylate after food. Transient hypotension has been reported following intravenous injection.

Porphyria. Etamsylate is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Pharmacokinetics

Etamsylate is absorbed from the gastrointestinal tract. It is excreted unchanged, mainly in the urine. Etamsylate is distributed into breast milk.

Uses and Administration

Etamsylate is a haemostatic that appears to maintain the stability of the capillary wall and correct abnormal platelet adhesion. It is given for the prophylaxis and control of haemorrhages from small blood vessels.

For short-term blood loss in menorrhagia a dose of 500 mg is given orally four times daily during menstruation. For the prophylaxis and treatment of periventricular haemorrhage in low birth-weight neonates 12.5 mg/kg is given by intramuscular or intravenous injection every 6 hours. For the control of haemorrhage after surgery etamsylate may be given orally to adults, or by intramuscular or intravenous injection in a dose of 250 to 500 mg; this dose may be repeated every 4 to 6 hours as necessary.

Menorrhagia. When given during menstruation to women with idiopathic menorrhagia (p.2126), etamsylate was as effective as mefenamic acid in reducing uterine blood loss in 1 study,[1] but was ineffective in another.[2] A review, which included published and unpublished results from these and 2 earlier studies, reported

that etamsylate produced about a 10 to 15% reduction in menstrual blood loss.[3] Etamsylate is now considered to be less effective than other treatments for menorrhagia, and is no longer recommended.[4]

1. Chamberlain G, *et al.* A comparative study of ethamsylate and mefenamic acid in dysfunctional uterine bleeding. *Br J Obstet Gynaecol* 1991; **98:** 707–11.
2. Bonnar J, Sheppard BL. Treatment of menorrhagia during menstruation: randomised controlled trial of ethamsylate, mefenamic acid, and tranexamic acid. *BMJ* 1996; **313:** 579–82.
3. Coulter A, *et al.* Treating menorrhagia in primary care: an overview of drug trials and a survey of prescribing practice. *Int J Technol Assess Health Care* 1995; **11:** 456–71.
4. National Collaborating Centre for Women's and Children's Health/NICE. Heavy menstrual bleeding (issued January 2007). Available at: http://www.nice.org.uk/nicemedia/pdf/CG44FullGuideline.pdf (accessed 06/03/08)

Neonatal intraventricular haemorrhage. Etamsylate is one of several drugs that have been tried in the prevention of intraventricular haemorrhage in very low birth-weight infants (p.1050). In a multicentre, placebo-controlled, double-blind study,[1] etamsylate was given in an initial dose of 12.5 mg/kg intravenously or intramuscularly within 1 hour of delivery, followed by the same dose intravenously every 6 hours for 4 days to a total dose of 200 mg/kg. Of 330 infants who had had no evidence of haemorrhage soon after delivery, the subsequent incidence of haemorrhage in the 162 who received etamsylate was reduced, particularly the more extensive grades when compared with the 168 who received placebo. Of a further 30 infants with evidence of periventricular haemorrhage before treatment, 21 were given etamsylate and 9 placebo; treatment with etamsylate limited the extension of bleeding. There was also a reduction in patent ductus arteriosus in the treated infants. However, a subsequent study using the same dosage regimen,[2] showed little benefit on short-term follow-up. It was considered that the study size may have been too small and the drug given too late; the initial dose was given within 4 hours of birth whereas, in the previous study, treatment was started within 1 hour of birth. Follow-up[3] of these infants at 2 years of age found that etamsylate had not reduced the risk of death, impairment, or disability. Developmental outcome assessments at about 4 years of age in patients from the first study[4] also found that despite the original reduction in intraventricular haemorrhage with etamsylate, it had not reduced cerebral palsy compared with the control group.

1. Benson JWT, *et al.* Multicentre trial of ethamsylate for prevention of periventricular haemorrhage in very low birthweight infants. *Lancet* 1986; **ii:** 1297–1300.
2. The EC Ethamsylate Trial Group. The EC randomised controlled trial of prophylactic ethamsylate for very preterm neonates: early mortality and morbidity. *Arch Dis Child* 1994; **70:** F201–F205.
3. Elbourne D, *et al.* Randomised controlled trial of prophylactic etamsylate: follow up at 2 years of age. *Arch Dis Child Fetal Neonatal Ed* 2001; **84:** F183–F187.
4. Schulte J, *et al.* Developmental outcome of the use of etamsylate for prevention of periventricular haemorrhage in a randomised controlled trial. *Arch Dis Child Fetal Neonatal Ed* 2005; **90:** F31–F35.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Impedil; ***Belg.:*** Dicynone; ***Braz.:*** Dicinone; ***Chile:*** Om-Dicynone†; ***Cz.:*** Dicynone; ***Fr.:*** Dicynone; ***Hung.:*** Dicynone; ***India:*** Alstat; Ethacid; Ethamcip; Ethasyl; Hemsyl; Revici-E; ***Indon.:*** Dicynone; ***Irl.:*** Dicynene; ***Ital.:*** Dicynone; Eselin; ***Mex.:*** Dicynone; ***Rus.:*** Dicynone (Дицинон); ***Singapore:*** Dicynone†; ***Spain:*** Dicinone; Hemo 141; ***Switz.:*** Dicynone; ***UK:*** Dicynene; ***Venez.:*** Dicynone.

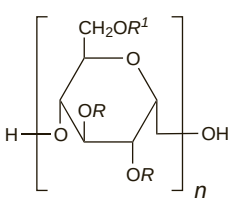
Etherified Starches ⊗

Almidón, éteres de; HES; Hydroxyethyl Starch; Hydroxyéthylamidon; Hydroxyethylamylum. 2-Hydroxyethyl ether starch.

CAS — 9005-27-0.

ATC — B05AA07.

ATC Vet — QB05AA07.



in which either *R* or R^1 may be either H or CH_2CH_2OH

(hetastarch)

Description. Etherified starches are starches that are composed of more than 90% of amylopectin and that have been etherified to varying extents.

- hetastarch (*BAN, USAN*): an average of 7 to 8 of the hydroxy groups in each 10 D-glucopyranose units of starch polymer have been converted into OCH_2CH_2OH groups
- pentastarch (*BAN, USAN*): an average of 4 to 5 of the hydroxy groups in each 10 D-glucopyranose units of the starch polymer have been converted to OCH_2CH_2OH groups

Etherified starches also vary in terms of average molecular weight and the position of etherification within the glucopyranose unit.

Incompatibility. Hetastarch is incompatible with many compounds including a number of injectable antibacterials.

References.

1. Wohlford JG, Fowler MD. Visual compatibility of hetastarch with injectable critical-care drugs. *Am J Hosp Pharm* 1989; **46:** 995–6.
2. Wohlford JG, *et al.* More information on the visual compatibility of hetastarch with injectable critical-care drugs. *Am J Hosp Pharm* 1990; **47:** 297–8.

Adverse Effects and Precautions

Hypersensitivity reactions including anaphylactic reactions have occurred after infusion of etherified starches. Pruritus can occur after long-term use of high doses of etherified starches; the onset may be delayed until weeks after the last infusion. Serum-amylase concentrations may appear to increase during infusion of etherified starches due to formation of an enzyme-substrate complex that is only eliminated slowly.

Precautions that should be observed with plasma expanders are described under Dextran 70, p.1060, and these should be considered when etherified starches are used. There may be some interference with blood grouping and cross-matching of blood.

◊ Reviews.

1. Wiedermann CJ. Hydroxyethyl starch - can the safety problems be ignored? *Wien Klin Wochenschr* 2004; **116:** 583–94.

Effects on the blood. Use of plasma expanders causes dilution of clotting factors and may also have direct effects on coagulation. Effects of etherified starches on the coagulation system include[1,2] a decrease in clotting factor VIII and von Willebrand factor that results in an acquired type I von Willebrand disease (see p.1051), a prolongation of the activated partial thromboplastin time, and a reduction in platelet volume. The extent of these effects appears to depend on the molecular weight and the rate of degradation *in vivo* of the starch. Etherified starches of high molecular weight that are more slowly degraded (due to a high degree of substitution or a high ratio of hydroxyethylation at the C2:C6 positions) have a greater effect on blood coagulation than medium and low molecular weight, easily degraded, etherified starches. Coagulopathy and haemorrhage have been reported with the use of solutions of etherified starches.[1,3] Serious complications such as intracranial bleeding and cerebral oedema have been reported in studies of patients with ischaemic stroke and other brain injuries who have been treated with etherified starches of various molecular weights and degrees of substitution, and several trials have been stopped prematurely as a result.[4]

1. Treib J, *et al.* Coagulation disorders caused by hydroxyethyl starch. *Thromb Haemost* 1997; **78:** 974–83.
2. de Jonge E, Levi M. Effects of different plasma substitutes on blood coagulation: a comparative review. *Crit Care Med* 2001; **29:** 1261–7.
3. Jonville-Béra A-P, *et al.* Acquired type I von Willebrand's disease associated with highly substituted hydroxyethyl starch. *N Engl J Med* 2001; **345:** 622–3.
4. Wiedermann CJ. Complications of hydroxyethyl starch in acute ischemic stroke and other brain injuries. *Pathophysiol Haemost Thromb* 2003; **33:** 225–8.

Effects on the kidneys. Osmotic-nephrosis-like lesions found at biopsy in some transplanted kidneys have been attributed to use of solutions of etherified starches in the donor patient.[1] Such use has also been reported to impair immediate graft function.[2] However, another study[3] found no association between the use of these solutions in the donor patient and osmotic-nephrosis-like lesions or delayed graft function. Oliguric acute renal failure and osmotic-nephrosis-like lesions occurred in a patient who was given an etherified starch infusion during surgery for carcinoma of the tonsils.[4]

Etherified starches should be used with caution in patients with renal impairment.[5]

1. Legendre CH, *et al.* Hydroxyethylstarch and osmotic-nephrosis-like lesions in kidney transplantation. *Lancet* 1993; **342:** 248–9.
2. Cittanova ML, *et al.* Effect of hydroxyethylstarch in brain-dead kidney donors on renal function in kidney-transplant recipients. *Lancet* 1996; **348:** 1620–22.
3. Coronel B, *et al.* Hydroxyethylstarch and renal function in kidney transplant recipients. *Lancet* 1997; **349:** 884.
4. De Labarthe A, *et al.* Acute renal failure secondary to hydroxyethylstarch administration in a surgical patient. *Am J Med* 2001; **111:** 417–18.
5. Boldt J. Hydroxyethylstarch as a risk factor for acute renal failure: is a change of clinical practice indicated? *Drug Safety* 2002; **25:** 837–46.

Effects on the skin. Pruritus has been reported after infusion of etherified starches.[1] It appears to be associated with tissue deposition of the starch although the actual mechanism by which this provokes pruritus is unresolved. The effect appears to be dose-related, which may explain the differences in reported incidences that have ranged from less than 10% to more than 60% of patients being affected. The molecular weight and degree of substitution of the etherified starch do not appear to be risk factors. The pruritus is usually generalised, but there are reports of localised pruritus affecting the trunk, extremities, anogenital area, and head and neck. It is frequently severe, persistent, and refractory to treatment, causing sleep disturbances and adversely affecting quality of life. Attacks of pruritus may be precipitated by heat, sweating, exercise, bathing, mechanical pressure, and mental stress. It typically has a delayed onset of 1 to 6 weeks after exposure to the etherified starch. Average durations of 9 to 15 weeks have been reported, but in some cases pruritus has continued for up to 2 years. The condition is generally unresponsive to treatment, although there have been reports of relief with topical capsaicin, ultraviolet therapy, or oral naltrexone.

Marked and persistent periocular swelling developed in a patient after 15 daily infusions of hetastarch.[2] Abnormal accumulation of hetastarch was found in the periocular tissues.

1. Bork K. Pruritus precipitated by hydroxyethyl starch: a review. *Br J Dermatol* 2005; **152:** 3–12.
2. Kiehl P, *et al.* Decreased activity of acid α-glucosidase in a patient with persistent periocular swelling after infusions of hydroxyethyl starch. *Br J Dermatol* 1998; **138:** 672–77.

Pharmacokinetics

Etherified starches consist of mixtures of molecules with a range of molecular weights and with varying degrees of etherification. After intravenous infusion the molecules with a molecular weight of less than 50 000 are readily excreted unchanged by the kidney; larger molecules are metabolised and eliminated more slowly. The rate of metabolism depends upon the size of the molecule and the degree and position of etherification, with a high molecular weight, high degree of etherification, and etherification predominantly at the C2 position leading to a slower rate of metabolism and hence a longer duration of action. About 33% of a dose of high-molecular-weight hetastarch (weight average molecular weight 450 000) and about 70% of a dose of medium-molecular-weight pentastarch (weight average molecular weight 250 000) is excreted in the urine in 24 hours. Etherified starches may be distributed to various tissues; a small proportion of the dose may persist in the body for several years.

◊ References.

1. Mishler JM, *et al.* Changes in the molecular composition of circulating hydroxyethyl starch following consecutive daily infusions in man. *Br J Clin Pharmacol* 1979; **7:** 505–9.
2. Mishler JM, *et al.* Post-transfusion survival of hydroxyethyl starch 450/0.70 in man: a long-term study. *J Clin Pathol* 1980; **33:** 155–9.
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Uses and Administration

Etherified starches are plasma volume expanders used in the management of hypovolaemic shock (p.1183). Those most commonly used include high-molecular-weight hetastarch (weight average molecular weight 450 000 to 480 000) and medium-molecular-weight pentastarch (weight average molecular weight 200 000 to 250 000). Other etherified starches that are used include low-molecular-weight pentastarch and medium-molecular-weight hexastarch, which has a degree of etherification between that of pentastarch and hetastarch. A higher molecular weight hetastarch is also available. Iso-oncotic solutions of etherified starches, for example, 6% hetastarch or 6% medium-molecular-weight pentastarch, exert a similar colloidal osmotic pressure to human albumin, and when given by intravenous infusion produce an expansion of plasma volume slightly in excess of the infused volume. Hyperoncotic solutions, for example 10% medium-molecular-weight pentastarch, produce an expansion of plasma volume of about 1.5 times the infused volume. The du-