Masoprocol *(USAN, rINN)*

CHX-10; CHX-100; Masoprocolum; Mesonordihydroguaiaretic Acid; *meso*-NDGA. *meso*-4,4′-(2,3-Dimethyltetramethylene)-dipyrocatechol.

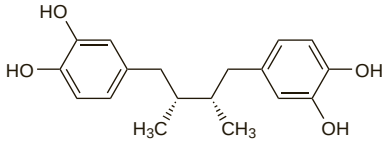
Мазопрокол

$C_{18}H_{22}O_4$ = 302.4.

CAS — 27686-84-6.

ATC — L01XX10.

ATC Vet — QL01XX10.



Profile

Masoprocol is a 5-lipoxygenase inhibitor isolated from the chaparral or creosote bush, *Larrea tridentata* (p.2280). It is reported to have antineoplastic activity. It has been used in the topical treatment of actinic (solar) keratoses. Local irritation and contact dermatitis have occurred.

Melanoma Vaccines

ATC — L03AX12.

Profile

A number of therapeutic vaccines designed to stimulate an antibody response are being developed for the treatment of melanoma (p.673).

One available preparation contains melanoma lysate (*Melacine*; *Schering, Canada*). It is used intramuscularly in a regimen with cyclophosphamide for the treatment of metastatic disease. Patients who show a clinical response may continue the melanoma vaccine as maintenance therapy. Adverse effects include injection site reactions such as granuloma formation, gastrointestinal disturbances, flu-like syndrome, and hypersensitivity reactions.

Other potential melanoma vaccines may be based on whole cells, GM2 ganglioside, heat shock proteins, or autologous tumour cells conjugated to an immunogenic hapten.

◊ Reviews.

1. Kim CJ, *et al.* Immunotherapy for melanoma. *Cancer Control* 2002; **9:** 22–30.
2. Minev BR. Melanoma vaccines. *Semin Oncol* 2002; **29:** 479–93.
3. Parmiani G, *et al.* Immunotherapy of melanoma. *Semin Cancer Biol* 2003; **13:** 391–400.
4. Sondak VK, Sosman JA. Results of clinical trials with an allogenic melanoma tumor cell lysate vaccine: Melacine. *Semin Cancer Biol* 2003; **13:** 409–15.
5. Castelli C, *et al.* Heat shock proteins: biological functions and clinical application as personalized vaccines for human cancer. *Cancer Immunol Immunother* 2004; **53:** 227–33.
6. Komenaka I, *et al.* Immunotherapy for melanoma. *Clin Dermatol* 2004; **22:** 251–65.
7. Oki Y, Younes A. Heat shock protein-based cancer vaccines. *Expert Rev Vaccines* 2004; **3:** 403–11.
8. Elliott B, Dalgleish A. Melanoma vaccines. *Hosp Med* 2004; **65:** 668–73.
9. Bystryn JC, Reynolds SR. Melanoma vaccines: what we know so far. *Oncology (Williston Park)* 2005; **19:** 97–108.
10. Saleh F, *et al.* Melanoma immunotherapy: past, present, and future. *Curr Pharm Des* 2005; **11:** 3461–73.
11. Lens M. The role of vaccine therapy in the treatment of melanoma. *Expert Opin Biol Ther* 2008; **8:** 315–23.
12. Rosenthal R, *et al.* Active specific immunotherapy phase III trials for malignant melanoma: systematic analysis and critical appraisal. *J Am Coll Surg* 2008; **207:** 95–105.

Preparations

Proprietary Preparations (details are given in Part 3)

Canad.: Melacine†.

Melphalan *(BAN, USAN, rINN)*

CB-3025; Melfalaani; Melfalán; Melfalan; Melphalanum; NSC-8806 (melphalan hydrochloride); PAM; Phenylalanine Mustard; Phenylalanine Nitrogen Mustard; L-Sarcolysine; WR-19813. 4-Bis(2-chloroethyl)amino-L-phenylalanine.

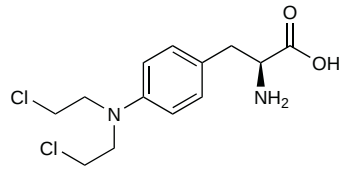
Мелфалан

$C_{13}H_{18}Cl_2N_2O_2$ = 305.2.

CAS — 148-82-3 (melphalan); 3223-07-2 (melphalan hydrochloride).

ATC — L01AA03.

ATC Vet — QL01AA03.



NOTE. Merphalan (CB-3007; NSC-14210; sarcolysine) is the racemic form of melphalan; Medphalan (CB-3026; NSC-35051) is the D-isomer of melphalan.

Pharmacopoeias. In *Br.*, *Jpn*, and *US*.

BP 2008 (Melphalan). A white or almost white powder. Practically insoluble in water, in chloroform, and in ether; slightly soluble in methyl alcohol; dissolves in dilute mineral acids. Protect from light.

USP 31 (Melphalan). An off-white to buff powder with a faint odour. Practically insoluble in water, in chloroform, and in ether; slightly soluble in alcohol and in methyl alcohol; soluble in dilute mineral acids. Store in airtight, glass containers. Protect from light.

Stability. A study of the stability of melphalan 40 and 400 micrograms/mL in infusion fluids reported that the time for a 10% loss of drug at 20° in sodium chloride 0.9% injection was 4.5 hours, compared with 2.9 hours in lactated Ringer's injection, which has a considerably lower chloride ion content, and only 1.5 hours in glucose 5% injection.[1] At 25° the corresponding figures were 2.4, 1.5, and 0.6 hours, and at 37° they were 0.6, 0.4, and 0.3 hours. It was concluded that melphalan is sufficiently stable at 20° in sodium chloride injection to permit infusion, but that increased temperature and decreased chloride ion concentration were associated with faster degradation rates.[1] Another study recommended that solutions of melphalan be handled at temperatures above 5° for the minimum time but found that a solution containing 20 micrograms/mL in sodium chloride 0.9% could be stored for at least 6 months at –20° without significant deterioration.[2] A more recent study, while recommending storage at 4° between preparation and use of the infusion, considered that giving it at a room temperature of 20° or below, and use of hypertonic (3%) saline as a diluent, would be sufficient to allow prolonged infusion.[3] The practicalities of such a procedure were not addressed.

1. Tabibi SE, Cradock JC. Stability of melphalan in infusion fluids. *Am J Hosp Pharm* 1984; **41:** 1380–2.
2. Bosanquet AG. Stability of melphalan solutions during preparation and storage. *J Pharm Sci* 1985; **74:** 348–51.
3. Pinguet F, *et al.* Effect of sodium chloride concentration and temperature on melphalan stability during storage and use. *Am J Hosp Pharm* 1994; **51:** 2701–4.

Adverse Effects and Treatment

For general discussions see Antineoplastics, p.635 and p.639.

The onset of neutropenia and thrombocytopenia is variable; the nadir of bone-marrow depression usually occurs at 2 to 3 weeks after starting treatment with melphalan, with recovery after 4 to 5 weeks.

Skin rashes and hypersensitivity reactions, including anaphylaxis, may occur. Cardiac arrest has been reported in association with such effects. Gastrointestinal disturbances may sometimes occur, particularly at high doses where diarrhoea, vomiting, and stomatitis may become dose-limiting. Haemolytic anaemia, vasculitis, pulmonary fibrosis, and hepatic disorders including hepatitis and jaundice have been reported. Suppression of ovarian function is common in premenopausal women; temporary or permanent sterility may occur in male patients. Extravasation of melphalan injection can cause skin ulceration and necrosis. As with other alkylating agents, melphalan also has carcinogenic, mutagenic, and teratogenic potential.

Mucositis. Amifostine has been shown to reduce the frequency and severity of melphalan-induced oral mucositis.[1]

1. Spencer A, *et al.* Prospective randomised trial of amifostine cytoprotection in myeloma patients undergoing high-dose melphalan conditioned autologous stem cell transplantation. *Bone Marrow Transplant* 2005; **35:** 971–7.

Overdosage. A 12-month old child given melphalan 140 mg intravenously (a tenfold overdose) developed pronounced lymphopenia within 24 hours but had no other significant adverse effects until the seventh day, when neutropenia, thrombocytopenia, oral ulceration, and diarrhoea developed.[1] Bone marrow recovered within 40 days. Treatment was by vigorous hyperalimentation and close surveillance during this period and the patient subsequently remained well 9 months afterwards, without complications. Cases of intravenous melphalan overdose have also been reported in adults,[2] resulting in bone-marrow depression, haemorrhagic diarrhoea, and electrolyte disturbances. Bone-marrow depression has also been reported after cumulative oral doses of 360 mg over 3 weeks,[3] and 560 mg over 2 weeks.[4] Filgrastim was used in one of these cases to stimulate bone-marrow recovery.[4]

1. Coates TD. Survival from melphalan overdose. *Lancet* 1984; **ii:** 1048.
2. Jost LM. Überdosierung von Melphalan (Alkeran): Symptome und Behandlung: eine Übersicht. *Onkologie* 1990; **13:** 96–101.
3. Grimes DJ, *et al.* Complete remission of paraproteinaemia and neuropathy following iatrogenic oral melphalan overdose. *Br J Haematol* 1993; **83:** 675–7.
4. Jirillo A, *et al.* Accidental overdose of melphalan per os in a 69-year-old woman treated for advanced endometrial carcinoma. *Tumori* 1998; **84:** 611.

Precautions

For general discussions see Antineoplastics, p.641.

Care is required in patients with impaired renal function.

Handling and disposal. *Urine and faeces* produced for up to 48 hours and 7 days respectively after a dose of melphalan by mouth should be handled wearing protective clothing.[1]

1. Harris J, Dodds LJ. Handling waste from patients receiving cytotoxic drugs. *Pharm J* 1985; **235:** 289–91.

Interactions

Use of nalidixic acid with high-dose intravenous melphalan in children has resulted in fatal haemorrhagic enterocolitis.

Ciclosporin. For reference to enhanced toxicity when melphalan was given with ciclosporin, see under Ciclosporin, p.1826.

Food. The bioavailability of oral melphalan is significantly reduced, by up to 45%, by food. Some recommend that melphalan should not be taken with food, and that if dosage is switched from after to before food patients should be monitored for increased toxicity.[1]

1. Nathan C, Betmouni R. Melphalan: avoid with food. *Pharm J* 1996; **257:** 264.

Interferons. The fever induced by interferon alfa resulted in a reduction in the area under the plasma concentration-time curve for melphalan in a study of 10 patients, although the peak plasma concentration and time to peak concentration were not affected.[1] The effect was thought to represent increased chemical reactivity of melphalan at the elevated temperature.

1. Ehrsson H, *et al.* Oral melphalan pharmacokinetics: influence of interferon-induced fever. *Clin Pharmacol Ther* 1990; **47:** 86–90.

Pharmacokinetics

Absorption of melphalan from the gastrointestinal tract is variable; the mean bioavailability is reported to be 56% but it may range from 25 to 89%. Absorption is reduced by the presence of food (see above). On absorption it is rapidly distributed throughout body water with a volume of distribution of about 0.5 litres/kg, and has been reported to be inactivated mainly by spontaneous hydrolysis. About 60 to 90% is bound to plasma proteins, mainly albumin. The terminal plasma half-life of melphalan has been reported to be of the order of 30 to 150 minutes. Melphalan is excreted in the urine, about 10% as unchanged drug.

◊ References.

1. Nath CE, *et al.* Melphalan pharmacokinetics in children with malignant disease: influence of body weight, renal function, carboplatin therapy and total body irradiation. *Br J Clin Pharmacol* 2005; **59:** 314–24.
2. Nath CE, *et al.* Population pharmacokinetics of melphalan in paediatric blood or marrow transplant recipients. *Br J Clin Pharmacol* 2007; **64:** 151–64.
3. Padussis JC, *et al.* Pharmacokinetics and drug resistance of melphalan in regional chemotherapy: ILP versus ILI. *Int J Hyperthermia* 2008; **24:** 239–49.

Uses and Administration

Melphalan is an antineoplastic that acts as a bifunctional alkylating agent. It is used mainly in the treatment of multiple myeloma. Melphalan has also been given to patients with carcinoma of the breast and ovary, neuroblastoma, Hodgkin's disease, and in polycythaemia vera, and has been given by intra-arterial regional perfusion for malignant melanoma and soft-tissue sarcomas. See also the cross-references given below. Melphalan is also used in the treatment of amyloidosis, see below.

Melphalan is usually given orally as a single daily dose or in divided doses; it is also given intravenously as the hydrochloride. Doses are calculated in terms of the base; 1.12 mg of melphalan hydrochloride is equiva-

lent to about 1 mg of melphalan. Frequent blood counts are essential and dosage should be adjusted according to haematological response. Therapy should be interrupted if the platelet or white cell count fall below acceptable levels (see also Bone-marrow Depression, p.639). It should be given with great caution if the neutrophil count has recently been depressed by chemotherapy or radiotherapy.

Numerous conventional-dose regimens have been tried for the treatment of multiple myeloma and there is still uncertainty as to the best schedule. Licensed **oral** dosage regimens include:

- 150 micrograms/kg daily in divided doses for 4 to 7 days
- 250 micrograms/kg daily for 4 days
- 6 mg daily for 2 to 3 weeks

Melphalan is usually combined with corticosteroids. Courses are followed by a rest period of up to 6 weeks to allow recovery of haematological function and are then repeated, or maintenance therapy may be instituted, usually with a daily dose of 1 to 3 mg, or up to 50 micrograms/kg. For optimum effect, therapy is usually adjusted to produce a moderate leucopenia, with white cell counts in the range 3000 to 3500 cells/mm^3.

In the treatment of breast cancer, licensed doses are 150 micrograms/kg daily or 6 mg/m^2 daily for 5 days, repeated every 6 weeks. Doses of 200 micrograms/kg daily for 5 days every 4 to 8 weeks have been given to patients with ovarian carcinoma.

In patients with polycythaemia vera, doses of 6 to 10 mg daily for 5 to 7 days, and then 2 to 4 mg daily, have been used for remission induction; a dose of 2 to 6 mg weekly has been used for maintenance.

Melphalan is also given **intravenously**; a single dose of 1 mg/kg, repeated in 4 weeks if the platelet and neutrophil counts permit, has been licensed in ovarian adenocarcinoma. It may be infused in sodium chloride 0.9% or injected into the tubing of a fast-running drip; when given by infusion the time from reconstitution of the solution to completion of infusion should not exceed 1.5 hours and prolonged infusions should be carried out with several batches of solution, each freshly prepared. In multiple myeloma, the licensed dose for use as a single agent is an intravenous dose of 400 micrograms/kg or 16 mg/m^2, infused over 15 to 20 minutes; the first 4 doses may be given at 2-week intervals, but further doses should be given at 4-week intervals depending on toxicity.

High-dose melphalan has been given intravenously in some malignancies: doses of 100 to 240 mg/m^2 have been licensed in neuroblastoma, and 100 to 200 mg/m^2 in multiple myeloma, generally followed by autologous stem cell rescue, which becomes essential where doses exceed 140 mg/m^2. High doses should be given through a central venous catheter.

Melphalan may be given by **local arterial perfusion** in the management of melanoma and soft-tissue sarcomas. A typical dosage range for upper extremity perfusions is 0.6 to 1 mg/kg, whereas for lower extremity perfusions doses of 0.8 to 1.5 mg/kg (in melanoma) or 1 to 1.4 mg/kg (in sarcoma) are typically used.

The dose of melphalan should be reduced in patients with **renal impairment** (see below).

Administration in renal impairment. The initial dose of intravenous melphalan should be reduced by about 50% in patients with renal impairment and dosage reduction should be considered when giving it by mouth. High-dose regimens are not recommended in patients with moderate to severe renal impairment.

Amyloidosis. Amyloidosis refers to a group of conditions characterised by accumulation of a waxy proteinaceous infiltrate within body tissues. Various forms are known,[1-3] including:

- primary or AL amyloidosis, in which the amyloid is derived from immunoglobulin light chains
- ATTR amyloidosis (a familial form), in which amyloid is derived from transthyretin
- AA amyloidosis, which is most often secondary to chronic inflammation, such as that associated with rheumatoid arthritis, tuberculosis, or familial Mediterranean fever (p.557)

Symptoms vary, depending on where the amyloid is deposited. The organs most commonly affected are the heart and kidneys. Renal amyloidosis can present as proteinuria, leading to nephrotic syndrome and renal failure. While renal disease is common in the AA and AL forms, it is less prevalent in ATTR amyloidosis, which commonly presents with neuropathy. Cardiac involvement, rare in AA amyloidosis, is variable in the ATTR form, and common in the AL form; it manifests as restrictive cardiomyopathy, leading to congestive heart failure. Painful peripheral sensory neuropathy and carpal tunnel syndrome also occur frequently. Amyloid deposition in the gastrointestinal tract can lead to malabsorption. Hepatomegaly is common. Macroglossia, due to deposition of amyloid in the tongue, occurs only in the AL form.[1,2]

Management depends to some extent upon the type of amyloidosis involved, and the site, but no drug or combination of drugs is unequivocally effective. Treatment for AA amyloidosis secondary to chronic inflammation is aimed at the underlying disease; immunosuppressants such as chlorambucil, cyclophosphamide, and methotrexate have been used, as well as inhibitors of tumour necrosis factor and interleukin-1 receptor antagonists.[4] Colchicine is effective in the treatment of AA amyloidosis complicating familial Mediterranean fever, but is not considered to be of benefit in other forms of amyloidosis.[1,5] Melphalan plus prednisone or prednisolone has been shown to increase median survival in primary amyloidosis patients.[6] It is considered the treatment of choice in AL amyloidosis for patients in whom more intensive chemotherapy is not appropriate; evidence of benefit from the addition of a corticosteroid has not been evaluated and in some patients, it may be reasonable not to include a corticosteroid.[5] Melphalan, prednisone, and colchicine was found to be more effective than colchicine alone in the treatment of AL amyloidosis,[7] but a later trial[8] found no benefit in adding colchicine to the standard therapy. Addition of multiple alkylating agents such as vincristine, carmustine, and cyclophosphamide to the standard therapy[9] did not improve survival or response. Evidence to support the use of alkylating-based combination chemotherapy for primary amyloidosis is lacking.[5] Alternatively, cycles of vincristine, doxorubicin, and dexamethasone (VAD) may be effective, but patients with cardiac amyloidosis may be at increased risk of anthracycline toxicity.[10] In the UK, VAD is considered as first-line therapy in patients under the age of 70 years who do not have cardiac failure, autonomic neuropathy, or peripheral neuropathy.[5] High-dose intravenous melphalan with autologous haematopoietic stem cell transplantation (HSCT) has been used;[11] it may result in complete remission of primary amyloidosis,[12-14] and some[1] consider it the treatment of choice. While this may improve renal disease,[12] the therapy remains very toxic, and patient selection on the basis of limited organ disease and no significant cardiac involvement, may reduce morbidity and mortality.[5,13] The outcome of treatment with high-dose intravenous melphalan with autologous HSCT was not superior to standard-dose oral melphalan plus oral dexamethasone in patients with newly diagnosed AL amyloidosis.[15] High-dose dexamethasone or thalidomide may be considered in patients in whom other regimens may not be feasible due to expected toxicity or in those refractory to chemotherapy;[5] good results have been reported in patients with AL amyloidosis given a regimen combining cyclophosphamide with dexamethasone and thalidomide.[16] Local application or oral dosage of dimethyl sulfoxide, and 4′-iodo-4′-deoxydoxorubicin has been investigated.[1,10]

Symptomatic management is also important. Care must be taken to avoid digitalis toxicity when cardiac amyloid is present, as well as to avoid salt and water depletion through injudicious use of diuretics. Calcium-channel blockers and beta blockers should be avoided.[1] Renal transplantation may be considered in end-stage renal failure due to amyloidosis, but unless amyloid production has been stopped disease is likely to recur in the new kidney. Cardiac transplantation, and subsequent chemotherapy with epirubicin, carmustine, and cyclophosphamide to suppress the underlying disease and control amyloid deposition in the graft has also been described.[17] Liver transplantation is the definitive therapy for patients with ATTR amyloidosis.[1,18] Because amyloid deposits contain a plasma glycoprotein serum amyloid P component (SAP) that contributes to the stability of the deposits, and thus contributes to the pathogenesis of amyloidosis, future therapeutic approaches include the targeting of SAP to deplete it from the tissues and clear it from the plasma. Ro-63-8695 (CPHPC) is being investigated.[3,19] Eprodisate disodium is under investigation for AA amyloidosis.[20]

1. Khan MF, Falk RH. Amyloidosis. *Postgrad Med J* 2001; **77:** 686–93.
2. Falk RH, Skinner M. The systemic amyloidoses: an overview. *Adv Intern Med* 2000; **45:** 107–37.
3. Gillmore JD, Hawkins PN. Drug Insight: emerging therapies for amyloidosis. *Nat Clin Pract Nephrol* 2006; **2:** 263–70.
4. Lachmann HJ, *et al.* Natural history and outcome in systemic AA amyloidosis. *N Engl J Med* 2007; **356:** 2361–71.
5. British Society for Haematology. Guidelines on the diagnosis and management of AL amyloidosis. *Br J Haematol* 2004; **125:** 681–700. Also available at: http://www.bcshguidelines.com/pdf/ALamyloidosis_210604.pdf (accessed 07/03/06)
6. Gertz MA, Rajkumar SV. Primary systemic amyloidosis. *Curr Treat Options Oncol* 2002; **3:** 261–71.
7. Skinner M, *et al.* Treatment of 100 patients with primary amyloidosis: a randomized trial of melphalan, prednisone, and colchicine versus colchicine only. *Am J Med* 1996; **100:** 290–8.
8. Kyle RA, *et al.* A trial of three regimens for primary amyloidosis: colchicine alone, melphalan and prednisone, and melphalan, prednisone, and colchicine. *N Engl J Med* 1997; **336:** 1202–7.
9. Gertz MA, *et al.* Prospective randomized trial of melphalan and prednisone versus vincristine, carmustine, melphalan, cyclophosphamide, and prednisone in the treatment of primary systemic amyloidosis. *J Clin Oncol* 1999; **17:** 262–7.
10. Sezer O, *et al.* New therapeutic approaches in primary systemic AL amyloidosis. *Ann Hematol* 2000; **79:** 1–6.
11. Sanchorawala V, Seldin DC. An overview of high-dose melphalan and stem cell transplantation in the treatment of AL amyloidosis. *Amyloid* 2007; **14:** 261–9.
12. Dember LM, *et al.* Effect of dose-intensive intravenous melphalan and autologous blood stem-cell transplantation on AL amyloidosis-associated renal disease. *Ann Intern Med* 2001; **134:** 746–53.
13. Comenzo RL, Gertz MA. Autologous stem cell transplantation for primary systemic amyloidosis. *Blood* 2002; **99:** 4276–82.
14. Skinner M, *et al.* High-dose melphalan and autologous stem-cell transplantation in patients with AL amyloidosis: an 8-year study. *Ann Intern Med* 2004; **140:** 85–93.
15. Jaccard A, *et al.* Myélome Autogreffe (MAG) and Intergroupe Francophone du Myélome (IFM) Intergroup. High-dose melphalan versus melphalan plus dexamethasone for AL amyloidosis. *N Engl J Med* 2007; **357:** 1083–93.
16. Wechalekar AD, *et al.* Safety and efficacy of risk-adapted cyclophosphamide, thalidomide, and dexamethasone in systemic AL amyloidosis. *Blood* 2007; **109:** 457–64.
17. Hall R, *et al.* Cardiac transplantation for AL amyloidosis. *BMJ* 1994; **309:** 1135–7.
18. Suhr OB, *et al.* Liver transplantation for hereditary transthyretin amyloidosis. *Liver Transpl* 2000; **6:** 263–76.
19. Pepys MB, *et al.* Targeted pharmacological depletion of serum amyloid P component for treatment of human amyloidosis. *Nature* 2002; **417:** 254–9.
20. Dember LM, *et al.* Eprodisate for AA Amyloidosis Trial Group. Eprodisate for the treatment of renal disease in AA amyloidosis. *N Engl J Med* 2007; **356:** 2349–60.

Bone disorders, non-malignant. Fibrogenesis imperfecta ossium is a rare progressive bone disease in which disorders of bone collagen and mineralisation, and subsequent abnormal bone structure, result in bone pain and fractures. A patient responded to treatment with melphalan 10 mg and prednisolone 20 or 30 mg daily, in 7-day courses every 2 months.[1,2] Another showed some improvement with intermittent 5-day courses of melphalan 10 mg daily and prednisolone 40 mg daily.[3] However, melphalan alone was reported to be ineffective in 2 other patients; both experienced bone-marrow depression.[3,4]

1. Stamp TCB, *et al.* Fibrogenesis imperfecta ossium: remission with melphalan. *Lancet* 1985; **i:** 582–3.
2. Ralphs JR, *et al.* Ultrastructural features of the osteoid of patients with fibrogenesis imperfecta ossium. *Bone* 1989; **10:** 243–9.
3. Carr AJ, *et al.* Fibrogenesis imperfecta ossium. *J Bone Joint Surg Br* 1995; **77:** 820–9.
4. Lafage-Proust M-H, *et al.* Fibrogenesis imperfecta ossium: ineffectiveness of melphalan. *Calcif Tissue Int* 1996; **59:** 240–4.

Malignant neoplasms. The important role played by melphalan in the management of multiple myeloma is discussed on p.658. Melphalan is also used as part of salvage regimens for relapsed Hodgkin's disease (see p.655), in ovarian cancer (p.670), and for local perfusion of melanoma (p.673).

Preparations

BP 2008: Melphalan Injection; Melphalan Tablets;
USP 31: Melphalan Tablets.

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

Mepolizumab *(USAN, rINN)*

Mépolizumab; Mepolizumabum; SB-240563. Immunoglobulin G1, anti-(human interleukin 5) (human-mouse monoclonal SB-240563 γ1-chain), disulfide with human-mouse monoclonal SB-240563 κ-chain, dimer.

Меполизумаб

CAS — 196078-29-2.

Profile

Mepolizumab is an anti-interleukin-5 monoclonal antibody. It is under investigation in the treatment of hypereosinophilic syndrome (chronic eosinophilic leukaemia), as well as eosinophilic oesophagitis, and asthma.

◊ References.

1. Leckie MJ, *et al.* Effects of an interleukin-5 blocking monoclonal antibody on eosinophils, airway hyper-responsiveness, and the late asthmatic response. *Lancet* 2000; **356:** 2144–8.
2. Plötz S-G, *et al.* Use of an anti-interleukin-5 antibody in the hypereosinophilic syndrome with eosinophilic dermatitis. *N Engl J Med* 2003; **349:** 2334–9.
3. Braun-Falco M, *et al.* Angiolymphoid hyperplasia with eosinophilia treated with anti-interleukin-5 antibody (mepolizumab). *Br J Dermatol* 2004; **151:** 1103–4.