Uses and Administration

Mitotane is an antineoplastic with a selective inhibitory action on adrenal cortex activity. It may also modify peripheral steroid metabolism. It is given in the treatment of inoperable adrenocortical tumours and has also been used in patients with Cushing's syndrome (p.2344). Dosing schedules vary. In the UK, mitotane is started at a dose of 2 to 3 g daily in patients with adrenocortical tumours, given orally in 2 or 3 divided doses, and preferably with meals. Doses may be reduced to 1 to 2 g daily after 2 months of treatment, or until a cumulative dose of 200 g, or in event of toxicity. If plasma monitoring is available, initial doses may be as high as 4 to 6 g daily in divided doses until a cumulative dose of 75 g is reached (over about 15 days). Children or adolescents may be given starting doses of 1.5 to 3.5 g/m^2 daily, in 2 or 3 divided doses, with meals; this is reduced after 2 to 3 months according to mitotane plasma concentrations. In the USA, the usual initial oral dosage is 2 to 6 g daily in 3 or 4 divided doses. Doses are usually increased to 9 to 10 g daily, unless adverse effects necessitate dose reduction. The maximum tolerated dose ranges from about 2 to 16 g daily. In some countries, mitotane may also be started at 9 to 10 g daily in 3 or 4 divided doses.

◊ A retrospective study involving 105 patients with adrenocortical carcinoma found the prognosis to be generally poor with a 5-year survival of 22% among 88 patients followed up.[1] Surgical resection was the treatment of choice; mitotane treatment had no effect on survival although 8 patients had transient tumour regression and it was of some benefit in controlling adrenal hypersecretion. However, others have previously reported improved survival in patients with adrenocortical carcinoma in whom mitotane serum concentrations were above 14 micrograms/mL, and some[2] have suggested that the poor results with mitotane in the retrospective study may have been due to low serum-mitotane concentrations (see Therapeutic Drug Monitoring, above). A further study[3] found mitotane to be of benefit only in patients with adrenocortical carcinoma undergoing palliative surgery, but of no additional benefit as an adjuvant therapy for survival amongst patients receiving curative surgical resection. However, a retrospective analysis[4] of adjuvant mitotane therapy after radical resection found that it significantly prolonged recurrence-free survival. A review[5] concluded that, although mitotane is recommended for patients with unresectable tumours, only about 35% of such tumours respond.

1. Luton J-P, *et al.* Clinical features of adrenocortical carcinoma, prognostic factors, and the effect of mitotane therapy. *N Engl J Med* 1990; **322:** 1195–1201.
2. Haak HR, *et al.* Mitotane therapy of adrenocortical carcinoma. *N Engl J Med* 1990; **323:** 758.
3. Icard P, *et al.* Adrenocortical carcinomas: surgical trends and results of a 253-patient series from the French Association of Endocrine Surgeons study group. *World J Surg* 2001; **25:** 891–7.
4. Terzolo M, *et al.* Adjuvant mitotane treatment for adrenocortical carcinoma. *N Engl J Med* 2007; **356:** 2372–80.
5. Wooten MD, King DK. Adrenal cortical carcinoma: epidemiology and treatment with mitotane and a review of the literature. *Cancer* 1993; **72:** 3145–55.

Preparations

USP 31: Mitotane Tablets.

Proprietary Preparations (details are given in Part 3)
Braz.: Lisodren; ***Canad.:*** Lysodren; ***Cz.:*** Lysodren; ***Denm.:*** Lysodren; ***Fin.:*** Lysodren; ***Fr.:*** Lysodren; ***Ger.:*** Lysodren; ***Gr.:*** Lysodren; ***Hong Kong:*** Lysodren; ***Neth.:*** Lysodren; ***Pol.:*** Lysodren; ***Spain:*** Lysodren; ***UK:*** Lysodren; ***USA:*** Lysodren.

Mitoxantrone Hydrochloride

(BANM, USAN, rINNM)

CL-232315; DHAD; Dihydroxyanthracenedione Dihydrochloride; Hidrocloruro de mitoxantrona; Mitoksantron Hidroklorür; Mitoksantronihydrokloridi; Mitoksantrono hidrochloridas; Mitoxantron dihydrochlorid; Mitoxantrone, chlorhydrate de; Mitoxantron-hidroklorid; Mitoxantronhydroklorid; Mitoxantroni Dihydrochloridum; Mitoxantroni hydrochloridum; Mitozantron Hidroklorür; Mitozantrone Hydrochloride; NSC-301739. 1,4-Dihydroxy-5,8-bis[2-(2-hydroxyethylamino)ethylamino]anthraquinone dihydrochloride.

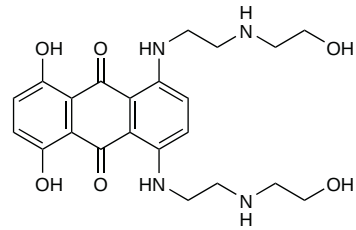
Митоксантрона Гидрохлорид

$C_{22}H_{28}N_4O_6,2HCl$ = 517.4.

CAS — 65271-80-9 (mitoxantrone); 70476-82-3 (mitoxantrone hydrochloride).

ATC — L01DB07.

ATC Vet — QL01DB07.



(mitoxantrone)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US.*
Ph. Eur. 6.2 (Mitoxantrone Hydrochloride). A dark-blue, electrostatic, hygroscopic powder. Sparingly soluble in water; practically insoluble in acetone; slightly soluble in methyl alcohol. Store in airtight containers.
USP 31 (Mitoxantrone Hydrochloride). A dark-blue powder. Sparingly soluble in water; practically insoluble in acetone, in acetonitrile, and in chloroform; slightly soluble in methyl alcohol. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for Doxorubicin, p.712. Mitoxantrone is reported to be better tolerated than doxorubicin. The nadir of the white cell count usually occurs about 10 days after a dose, with recovery by day 21. Elevation in liver enzyme values may occur; there are occasional reports of severe hepatic impairment in patients with leukaemia, in whom doses are generally higher and adverse effects of mitoxantrone may be more frequent and severe.

Transient blue-green coloration of the urine, and occasionally the sclerae, may occur. Tissue necrosis is rare after extravasation.

Severe neurotoxicity has resulted from erroneous intrathecal dosage; local or regional neuropathy has followed intra-arterial injection. Care is required in patients with pre-existing heart disease, or who have had prior anthracycline treatment or radiotherapy to the chest, as they are at increased risk of cardiotoxicity; regular cardiac examinations should be performed in such patients and in those who receive a total cumulative dose of mitoxantrone in excess of 160 mg/m^2. Care is also required in patients with hepatic impairment. Regular blood counts should be performed during treatment.

Alopecia. Two patients receiving therapy with mitoxantrone developed selective alopecia of white but not of dark hair.[1]

1. Arlin ZA, *et al.* Selective alopecia with mitoxantrone. *N Engl J Med* 1984; **310:** 1464.

Breast feeding. Mitoxantrone was detected in the breast milk of a woman with acute promyelocytic leukaemia in remission who was given consolidation chemotherapy that included mitoxantrone 6 mg/m^2 on days 1 to 3. Concentrations were 120 nanograms/mL just after the third dose and 18 nanograms/mL 28 days after treatment. Although she breast fed her neonate from 3 weeks after the completion of the course of treatment and no adverse effects were seen, the authors recommended that women treated with mitoxantrone should not breast feed.[1]

1. Azuno Y, *et al.* Mitoxantrone and etoposide in breast milk. *Am J Hematol* 1995; **48:** 131–2.

Effects on the heart. Data from over 4000 patients treated with mitoxantrone included 172 reports of cardiac events, including 42 cases of congestive heart failure and 66 of decreased ejection fraction.[1] Previous anthracycline therapy increased the risk, and congestive heart failure seemed to be more likely in patients exposed to a cumulative mitoxantrone dose of 160 mg/m^2, or 100 mg/m^2 in those already given anthracyclines. In a further 78 patients,[2] clinical heart failure developed in 2 after cumulative doses of 174 and 243 mg/m^2. Four of 9 other patients given mitoxantrone in doses above 100 mg/m^2 showed signs of cardiotoxicity, and a further patient previously given doxorubicin 313 mg/m^2 had a fall in stress ejection fraction after only 47 mg/m^2 of mitoxantrone. However, sinus bradycardia has also been reported[3] in 2 previously untreated patients after starting continuous infusions of mitoxantrone 10 mg/m^2. For information on the cardiotoxicity of anthracyclines, to which mitoxantrone is structurally related, see under Adverse Effects and Treatment of Doxorubicin, p.713.

1. Crossley RJ. Clinical safety and tolerance of mitoxantrone. *Semin Oncol* 1984; **11:** (suppl 1): 54–8.
2. Stuart-Harris R, *et al.* Cardiotoxicity associated with mitoxantrone. *Lancet* 1984; **ii:** 219–20.
3. Benekli M, *et al.* Mitoxantrone-induced bradycardia. *Ann Intern Med* 1997; **126:** 409.

Handling and disposal. *Urine and faeces* produced for up to 7 days after a dose of mitoxantrone 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.

Hypersensitivity. In a report of 3 patients, allergic-type reactions to mitoxantrone included vasculitis, facial oedema and skin rashes, and in one, breathlessness, tachypnoea, cyanosis, and unrecordable pulse and blood pressure.[1] Allergic reactions to the drug appear to be rare.

1. Taylor WB, *et al.* Allergic reactions to mitoxantrone. *Lancet* 1986; **i:** 1439.

Interactions

For a report of the effect of ciclosporin in patients receiving mitoxantrone and etoposide, see p.719.

Pharmacokinetics

After intravenous doses mitoxantrone is rapidly and extensively distributed to body tissues, and slowly excreted in urine and bile as unchanged drug and metabolites. The elimination half-life is reported to range from 5 to 18 days. Between 6 and 11% of a dose has been recovered from urine, and 13 to 25% in faeces, within 5 days. It does not appear to cross the blood-brain barrier, but it is distributed into breast milk.

◊ References.

1. Ehninger G, *et al.* Pharmacokinetics and metabolism of mitoxantrone: a review. *Clin Pharmacokinet* 1990; **18:** 365–80.

Uses and Administration

Mitoxantrone is an antineoplastic structurally related to doxorubicin (p.712). Its mode of action has not been fully established but it inhibits topoisomerase II and causes DNA strand breakage, as well as intercalating with DNA. It is cell-cycle non-specific but is most active against cells in the late S phase.

It is used in the treatment of metastatic breast cancer (p.661), and of non-Hodgkin's lymphomas (p.656), alone or with other agents. It may also be given to treat adult acute myeloid leukaemias (p.652). Mitoxantrone has also been used in patients with hormone-refractory prostate cancer (p.671), liver cancer (p.667), and ovarian cancer (p.670).

In addition, mitoxantrone is used in the management of secondary progressive or relapsing multiple sclerosis (see below), to reduce neurological disability or the frequency of relapses.

Mitoxantrone is given as the hydrochloride, but doses are expressed in terms of the base; 1.2 mg of the hydrochloride is equivalent to about 1 mg of mitoxantrone. In the treatment of breast cancer, prostate cancer, liver cancer, and lymphomas, a dose equivalent to mitoxantrone 14 mg/m^2 is given initially, then repeated every 3 weeks. It is diluted to at least 50 mL in sodium chloride 0.9% or glucose 5% and injected over at least 3 minutes into a freely-running intravenous infusion of either. Subsequent doses may be adjusted according to the degree of myelosuppression produced. Initial dosage may need to be reduced to 12 mg/m^2 in debilitated patients or those who have had previous chemotherapy. Doses should also probably be reduced when mitoxantrone is given as part of a combination regimen: an initial dose of 10 to 12 mg/m^2 has been suggested.

In the treatment of patients with acute myeloid leukaemia a dose of 12 mg/m^2 daily for 5 days may be given to induce remission; alternatively a similar dose may be given for 3 days with cytarabine.

Cardiac examinations are recommended in all patients who receive a cumulative dose of mitoxantrone greater than 160 mg/m^2; left ventricular ejection fraction (LVEF) should be determined before each dose in patients who have received a cumulative dose in excess of 100 mg/m^2. Regular blood counts should be per-

formed during treatment and courses should not be repeated until blood counts have recovered (see also Bone-marrow Depression, p.639).

In the management of multiple sclerosis, the recommended dose is the equivalent of mitoxantrone 12 mg/m^2 by intravenous infusion over 5 to 15 minutes. This dose may be given once every 3 months initially provided that neutrophil counts are above 1500 cells/mm^3 and that LVEF is greater than 50%. Blood counts should be monitored before each dose. LVEF should be evaluated before beginning mitoxantrone therapy and before all subsequent doses; a total cumulative lifetime dose in excess of 140 mg/m^2 should be avoided. LVEF should also be measured if signs or symptoms of heart failure develop.

◊ References.

1. Faulds D, *et al.* Mitoxantrone: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in the chemotherapy of cancer. *Drugs* 1991; **41:** 400–49.
2. Fox EJ. Mechanism of action of mitoxantrone. *Neurology* 2004; **63** (suppl): S15–S18.

Multiple sclerosis. Mitoxantrone has produced clear benefit[1-4] in terms of reduced relapse rate and a slowing of disease progression in patients with multiple sclerosis (p.892). It has been given intravenously in doses of 5 or 12 mg/m^2 every 3 months, or 8 mg/m^2 every month. Patients with progressive relapsing disease may benefit from rapid induction with 12 mg/m^2 monthly for 3 months.[5] Benefit has also been shown in combination with corticosteroids,[6] although the combination was not compared with mitoxantrone alone. However, cardiotoxicity limits the dose that can be given.[7,8] Because of this and other adverse effects, such as possible secondary malignancy or potentially permanent amenorrhoea, some consider the use of mitoxantrone in multiple sclerosis to be unproven[9] and others have cautioned[10] that it should not be used before other immunomodulators. A systematic review[11] concluded that mitoxantrone was moderately effective in the short-term treatment of multiple sclerosis, but that information on its long-term effects was lacking; use should be limited to patients with worsening relapsing-remitting or secondary progressive disease with evidence of worsening disability.

1. Millefiorini E, *et al.* Randomized placebo-controlled trial of mitoxantrone in relapsing-remitting multiple sclerosis: 24-month clinical and MRI outcome. *J Neurol* 1997; **244:** 153–9.
2. van de Wyngaert FA, *et al.* A double-blind clinical trial of mitoxantrone versus methylprednisolone in relapsing, secondary progressive multiple sclerosis. *Acta Neurol Belg* 2001; **101:** 210–16.
3. Hartung H-P, *et al.* Mitoxantrone in progressive multiple sclerosis: a placebo-controlled, double-blind, randomised, multicentre trial. *Lancet* 2002; **360:** 2018–25.
4. Jeffery DR, Herndon R. Review of mitoxantrone in the treatment of multiple sclerosis. *Neurology* 2004; **63** (suppl): S19–S24.
5. Rizvi SA, *et al.* Mitoxantrone for multiple sclerosis in clinical practice. *Neurology* 2004; **63** (suppl): S25–S27.
6. Edan G, *et al.* Therapeutic effect of mitoxantrone combined with methylprednisolone in multiple sclerosis: a randomised multicentre study of active disease using MRI and clinical criteria. *J Neurol Neurosurg Psychiatry* 1997; **62:** 112–118.
7. Ghalie RG, *et al.* Cardiac adverse effects associated with mitoxantrone (Novantrone) therapy in patients with MS. *Neurology* 2002; **59:** 909–13.
8. Cohen BA, Mikol DD. Mitoxantrone treatment of multiple sclerosis: safety considerations. *Neurology* 2004; **63** (suppl): S28–S32.
9. Chaudhuri A, Behan PO. Mitoxantrone trial in multiple sclerosis. *Lancet* 2003; **361:** 1133–4.
10. Goodin DS, *et al.* The use of mitoxantrone (Novantrone) for the treatment of multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2003; **61:** 1332–8.
11. Martinelli Boneschi F, *et al.* Mitoxantrone for multiple sclerosis. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 01/03/06).

Preparations

BP 2008: Mitoxantrone Intravenous Infusion;
USP 31: Mitoxantrone Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: Batinel; Micraleve; Mitoxgen; Mitoxmar; ***Austral.:*** Novantrone; Onkotrone; ***Austria:*** Novantron; ***Belg.:*** Novantrone; Xantrosin; ***Braz.:*** Misostol; Mitaxis†; Mitoxal; ***Canad.:*** Novantrone†; ***Chile:*** Neotalem†; ***Cz.:*** Novantrone†; Onkotrone; Refador; ***Denm.:*** Novantrone; ***Fin.:*** Novantrone; ***Fr.:*** Elsep; Novantrone; ***Ger.:*** Neoxantron; Novantron; Onkotrone; Onkoxantron; Ralenova; ***Gr.:*** Genefadrone; Mitoxan; Novantrone; Zyneva; ***Hong Kong:*** Novantrone; ***Hung.:*** Novantrone; Onkotrone; Refador; ***India:*** Oncotron; ***Indon.:*** Norexan; ***Irl.:*** Novantrone; ***Israel:*** Novantrone; ***Ital.:*** Novantrone; Onkotrone; ***Malaysia:*** Novantrone†; ***Mex.:*** Formyxan; Mitoxgen; Mitroxone; Neotalem; ***Neth.:*** Novantrone†; ***Norw.:*** Novantrone; ***NZ:*** Novantrone; ***Philipp.:*** Domitrone; Onkotrone; ***Port.:*** Mitroxene; Novantrone; ***S.Afr.:*** Novantrone; ***Singapore:*** Novantrone; ***Spain:*** Novantrone; Pralifan; ***Swed.:*** Novantrone; ***Switz.:*** Novantron; ***Thai.:*** Neotalem; Novantrone†; ***Turk.:*** Neotalem; Novantrone; ***UK:*** Novantrone†; Onkotrone; ***USA:*** Novantrone; ***Venez.:*** Misostol.

Multialchilpeptide

Multialquilpéptido.

CAS — 9076-25-9.

Profile

Multialchilpeptide is a complex of metamelfalan, an analogue of melphalan (p.742), with peptides. It has been used in the treatment of malignant neoplasms of the blood and lymphatic systems.

Naptumomab Estafenatox *(rINN)*

ABR-217620; Naptumomab Estafénatox; Naptumomabum Estafenatoxum. Immunoglobulin fragment, anti-[trophoblast glycoprotein (TPBG, 5T4)] monoclonal 5T4 gamma1 heavy chain fragment fusion protein [*Mus musculus* VH (5T4V14: H41>P, S44>G, I69>T, V113>G)-IGHG1_CH1] - [Glycyl-Glycyl-Prolyl] - superantigen SEA/E-120 (synthetic), non-disulfide linked with monoclonal 5T4 kappa light chain [*Mus musculus* V-KAPPA (5T4V18: F10>S, T45>K, I63>S, F73>L, T77>S, L78>V, L83>A)-IGKC].

Наптумомаб Эстафенатокс

CAS — 676258-98-3.

Profile

Naptumomab estafenatox is a murine monoclonal antibody conjugated with a bacterial superantigen, a modified variant of Staphylococcal enterotoxin A that acts as a target for T-cell activation. The antibody is directed against a tumour-specific antigen 5T4. Naptumomab estafenatox is under investigation for the treatment of renal cell carcinoma.

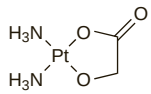
Nedaplatin *(rINN)*

Nédaplatine; Nedaplatino; Nedaplatinum. *cis*-Diammine(glycolato-O^1,O^2)platinum.

Недаплатин

$C_2H_8N_2O_3Pt$ = 303.2.

CAS — 95734-82-0.



Profile

Nedaplatin is a platinum derivative with general properties similar to those of cisplatin (p.698) although it may be associated with less nephrotoxicity. It is used in the treatment of a variety of malignant neoplasms. It is given by intravenous infusion over 1 hour or more, dissolved in at least 300 mL of an appropriate infusion solution, in doses of 80 to 100 mg/m^2. The infusion should be followed by infusion of at least 1 litre of fluid to ensure adequate hydration and reduce the risk of renal damage.

◊ References.

1. Yoshioka T, *et al.* A new combination chemotherapy with cis-diammine-glycolatoplatinum (Nedaplatin) and 5-fluorouracil for advanced esophageal cancers. *Intern Med* 1999; **38:** 844–8.
2. Adachi S, *et al.* Intravenous nedaplatin and intraarterial cisplatin with transcatheter arterial embolization for patients with locally advanced uterine cervical cancer. *Int J Clin Pharmacol Res* 2001; **21:** 105–10.
3. Kato H, *et al.* Efficacy and toxicity of nedaplatin and 5-FU with radiation treatment for advanced esophageal carcinomas. *Anticancer Res* 2003; **23:** 3493–8.
4. Ishibashi T, *et al.* Determination of optimal dosage for nedaplatin based on pharmacokinetic and toxicodynamic analysis. *Anticancer Res* 2005; **25:** 1273–81.
5. Shirai T, *et al.* Phase II study of the combination of gemcitabine and nedaplatin for advanced non-small-cell lung cancer. *Lung Cancer* 2006; **52:** 181–7.
6. Fuwa N, *et al.* Chemoradiation therapy using radiotherapy, systemic chemotherapy with 5-fluorouracil and nedaplatin, and intra-arterial infusion using carboplatin for locally advanced head and neck cancer–Phase II study. *Oral Oncol* 2007; **43:** 1014–20.
7. Oshita F, *et al.* Phase II study of nedaplatin and irinotecan followed by gefitinib for elderly patients with unresectable non-small cell lung cancer. *Cancer Chemother Pharmacol* 2008; **62:** 465–70.
8. Yokoyama Y, *et al.* A phase II multicenter trial of concurrent chemoradiotherapy with weekly nedaplatin in advanced uterine cervical carcinoma: Tohoku Gynecologic Cancer Unit Study. *Oncol Rep* 2008; **19:** 1551–6.

Preparations

Proprietary Preparations (details are given in Part 3)

Jpn: Aqupla.

Nelarabine *(BAN, USAN, rINN)*

GW-506U; GW-506U78; MAY; Nelarabina; Nélarabine; Nelarabinum; Nelzarabine; 506U; 506U78. 2-Amino-9-β-D-arabinofuranosyl-6-methoxy-9*H*-purine.

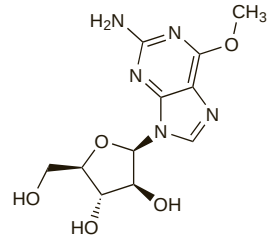
Неларабин

$C_{11}H_{15}N_5O_5$ = 297.3.

CAS — 121032-29-9.

ATC — L01BB07.

ATC Vet — QL01BB07.



Adverse Effects, Treatment, and Precautions

Neurotoxicity is common with nelarabine and may be dose-limiting. Signs and symptoms include somnolence, confusion, convulsions, ataxia, paraesthesias, and hypoaesthesia. Severe toxicity can manifest as coma, status epilepticus (which may be fatal), craniospinal demyelination, or ascending neuropathy. Risk of neurotoxicity is increased by previous or current intrathecal chemotherapy or previous radiation to the spine or brain. Leucopenia, thrombocytopenia, anaemia, and neutropenia are common, especially in children. Full blood counts should be regularly monitored. Other common adverse events include fatigue, gastrointestinal disorders, respiratory disorders, pyrexia, headache, hypokalaemia, hypoalbuminaemia, hyperbilirubinaemia, and increased liver enzyme values. Fatal cerebral haemorrhage has been reported. Appropriate measures to avoid hyperuricaemia (especially in patients considered at risk for tumour lysis syndrome) include adequate hydration, urinary alkalinisation, and possible prophylaxis with allopurinol.

Pharmacokinetics

In adult patients with leukaemia or lymphoma, nelarabine is rapidly eliminated from the plasma, with a half-life of about 30 minutes; no data are available for paediatric patients although the mean clearance is reported to be about 30% higher in children. Nelarabine is rapidly and extensively converted by demethylation to the active metabolite 9-β-D-arabinofuranosylguanine (ara-G; arabinosylguanine; arabinofuranosylguanine; guanine arabinoside); both nelarabine and ara-G are widely distributed throughout the body. Ara-G has an elimination half-life from plasma of about 3 hours. Plasma protein binding is not significant. Nelarabine also undergoes hydrolysis to form methylguanine. Both methylguanine and ara-G undergo further metabolism to guanine, which is deaminated to form xanthine, itself further oxidised to uric acid. Nelarabine and ara-G are partially eliminated by the kidneys; mean apparent clearance is lower in patients with mild to moderate renal impairment.

◊ References.

1. Kisor DF, *et al.* Pharmacokinetics of nelarabine and 9-beta- -arabinofuranosyl guanine in pediatric and adult patients during a phase I study of nelarabine for the treatment of refractory hematologic malignancies. *J Clin Oncol* 2000; **18:** 995–1003.

Uses and Administration

Nelarabine is a prodrug of ara-G, a purine nucleoside analogue that is used as an antimetabolite antineoplastic in the treatment of relapsed or refractory T-cell acute lymphoblastic leukaemia and lymphoma. A dose of 1.5 g/m^2 is given undiluted by intravenous infusion over 2 hours in adults, on days 1, 3, and 5 of a 21-day cycle. In children, nelarabine is given undiluted by in-