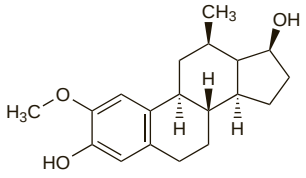
2-Methoxyoestradiol

2-ME2; 2-Methoxyestradiol; NSC-659853. (17β)-2-Methoxyestra-1,3,5(10)-triene-3,17-diol.

$C_{19}H_{26}O_3$ = 302.4.

CAS — 362-07-2.



Profile

2-Methoxyoestradiol is a metabolite of oestradiol (p.2097). It does not exhibit direct oestrogenic activity, but works through multiple cellular pathways to produce antineoplastic effects, including inhibition of angiogenesis and induction of apoptosis. 2-Methoxyoestradiol is under investigation in the treatment of various diseases, including glioblastoma, multiple myeloma, carcinoid tumours, as well as ovarian, prostate, breast, and renal cell cancers. It is also under investigation for pulmonary arterial hypertension.

Mifamurtide *(rINN)*

Mifamurtida; Mifamurtidum; MTP-PE; Muramyl Tripeptide Phosphatidyl Ethanolamine; Muramyl Tripeptide Phosphatidyl Monoethanolamine. 2-[(*N*-{(2*R*)-[(2-Acetamido-2,3-dideoxy-D-glucopyranos-3-yl)oxy]propanoyl}-L-alanyl-D-isoglutaminyl-L-alanyl)amino]ethyl (2*R*)-2,3-bis(hexadecanoyloxy)propyl hydrogen phosphate.

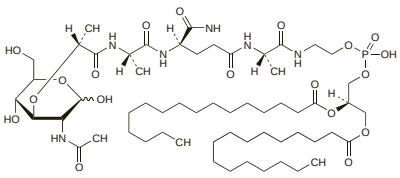
Мифамуртид

$C_{59}H_{109}N_6O_{19}P$ = 1237.5.

CAS — 83461-56-7.

ATC — L03AX15.

ATC Vet — QL03AX15.



NOTE. The name Mifamurtide has been used for both the base and the sodium salt.

Mifamurtide Sodium *(rINNM)*

CGP-19835A; L-MTP-PE (liposomal mifamurtide sodium); Mifamurtida sódica; Mifamurtide *(USAN)*; Mifamurtide Sodique; Mifamurtidum Natricum. 2-[(*N*-{(2*R*)-2-[(3*R*,4*R*,5*S*,6*R*)-3-(Acetylamino)-2,5-dihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-4-yloxy]propanoyl}-L-alanyl-D-isoglutaminyl-L-alanyl)amino]ethyl (2*R*)-2,3-bis(hexanoyloxy)propyl sodium phosphate hydrate.

Мифамуртид Натрий

$C_{59}H_{108}N_6NaO_{19}P.xH_2O$.

CAS — 838853-48-8.

NOTE. The name Mifamurtide has been used for both the base and the sodium salt.

Profile

Mifamurtide is an immunomodulator that activates macrophages to increase their capacity to destroy cancer cells. It is under investigation for the treatment of osteosarcoma.

Miltefosine *(BAN, rINN)*

D-18506; HDPC; Hexadecylphosphocholine; Miltefosiini; Miltefosin; Miltefosina; Miltéfosine; Miltefosinum. [2-(Trimethylammonio)ethyl][hexadecyloxyphosphonate].

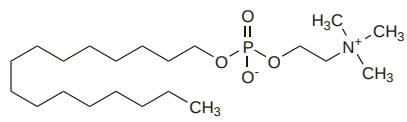
Мильтефозин

$C_{21}H_{46}NO_4P$ = 407.6.

CAS — 58066-85-6.

ATC — L01XX09.

ATC Vet — QL01XX09.



Profile

Miltefosine is a phospholipid derivative which is structurally related to the phospholipid components of the cell membrane and is thought to exert its antineoplastic actions by disruption of cell-membrane function. A 6% solution is applied once or twice daily as a topical antineoplastic agent for skin metastases of breast cancer. Miltefosine has also been tried orally for various malignant neoplasms. It is used for the treatment of visceral and cutaneous leishmaniasis in an oral dose of 1.5 to 2.5 mg/kg daily (maximum daily dose 150 mg) for 28 days.

Leishmaniasis. Miltefosine, given orally in doses of 50 to 150 mg daily, or about 2.5 mg/kg daily, for 28 days, appears to be of benefit[1-7] in the treatment of visceral leishmaniasis (p.824), and has been licensed for this purpose in India and Germany. Benefit has also been reported in patients given similar doses for New World cutaneous leishmaniasis,[8] and it has also been licensed in some South American countries, but success may depend on the infecting *Leishmania* species.[9] The use of longer courses of miltefosine in the treatment of patients with both leishmaniasis and HIV infection has been reported.[10]

1. Sundar S, *et al.* Trial of oral miltefosine for visceral leishmaniasis. *Lancet* 1998; **352:** 1821–3.
2. Jha TK, *et al.* Miltefosine, an oral agent, for the treatment of Indian visceral leishmaniasis. *N Engl J Med* 1999; **341:** 1795–1800.
3. Thakur CP, *et al.* Miltefosine in a case of visceral leishmaniasis with HIV co-infection; and rising incidence of this disease in India. *Trans R Soc Trop Med Hyg* 2000; **94:** 696–7.
4. Sundar S, *et al.* Short-course of oral miltefosine for treatment of visceral leishmaniasis. *Clin Infect Dis* 2000; **31:** 1110–13.
5. Sundar S, *et al.* Oral miltefosine for Indian visceral leishmaniasis. *N Engl J Med* 2002; **347:** 1739–46.
6. Bhattacharya SK, *et al.* Efficacy and tolerability of miltefosine for childhood visceral leishmaniasis in India. *Clin Infect Dis* 2004; **38:** 217–21.
7. Ritmeijer K, *et al.* A comparison of miltefosine and sodium stibogluconate for treatment of visceral leishmaniasis in an Ethiopian population with high prevalence of HIV infection. *Clin Infect Dis* 2006; **43:** 357–64.
8. Soto J, *et al.* Treatment of American cutaneous leishmaniasis with miltefosine, an oral agent. *Clin Infect Dis* 2001; **33:** e57–e61. Available at: http://www.journals.uchicago.edu/doi/pdf/10.1086/322689 (accessed 01/08/08)
9. Soto J, *et al.* Miltefosine for new world cutaneous leishmaniasis. *Clin Infect Dis* 2004; **38:** 1266–72.
10. Sindermann H, *et al.* Oral miltefosine for leishmaniasis in immunocompromised patients: compassionate use in 39 patients with HIV infection. *Clin Infect Dis* 2004; **39:** 1520–3.

Malignant neoplasms. References to the use of topical miltefosine in breast cancer.

1. Terwogt JM, *et al.* Phase II trial of topically applied miltefosine solution in patients with skin-metastasized breast cancer. *Br J Cancer* 1999; **79:** 1158–61.
2. Smorenburg CH, *et al.* Phase II study of miltefosine 6% solution as topical treatment of skin metastases in breast cancer patients. *Anticancer Drugs* 2000; **11:** 825–8.
3. Leonard R, *et al.* Randomized, double-blind, placebo-controlled, multicenter trial of 6% miltefosine solution, a topical chemotherapy in cutaneous metastases from breast cancer. *J Clin Oncol* 2001; **19:** 4150–9.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Mitex†; ***Austria:*** Miltex; ***Braz.:*** Miltex; ***Chile:*** Miltex†; ***Cz.:*** Miltex†; ***Fin.:*** Miltex†; ***Fr.:*** Miltex; ***Ger.:*** Impavido; Miltex; ***Hung.:*** Miltex; ***Israel:*** Miltex; ***Ital.:*** Miltex; ***Malaysia:*** Miltex†; ***Philipp.:*** Miltex; ***Singapore:*** Miltex; ***Spain:*** Miltex; ***Swed.:*** Miltex; ***UK:*** Miltex.

Mitobronitol *(BAN, rINN)*

DBM; Dibromomannitol; Mitobronitolum; NSC-94100; R-54; WR-220057. 1,6-Dibromo-1,6-dideoxy-D-mannitol.

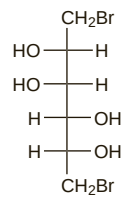
Митобронитол

$C_6H_{12}Br_2O_4$ = 308.0.

CAS — 488-41-5.

ATC — L01AX01.

ATC Vet — QL01AX01.



Pharmacopoeias. In *Br.*

BP 2008 (Mitobronitol). A white or almost white crystalline solid. Slightly soluble in water, in alcohol, and in acetone; practically insoluble in chloroform. Protect from light.

Profile

Mitobronitol is an antineoplastic which appears to act as an alkylating agent, perhaps by epoxide formation. It has been used in the management of thrombocythaemia, both primary, and secondary to chronic myeloid leukaemia or polycythaemia vera.

The usual oral dose is 250 mg daily until the platelet count falls to acceptable levels. Intermittent dosage has been given for maintenance therapy, adjusted according to the blood count. Frequent examination of the blood should be performed during treatment.

Mitobronitol is well absorbed from the gastrointestinal tract and is excreted through the liver into the bile, with reabsorption from the small intestine. It is eliminated as unchanged drug and some bromine-containing metabolites in the urine over several days.

Carcinogenicity. Long-term follow-up of a cooperative study[1] involving 350 patients with polycythaemia vera and treated with mitobronitol was thought to indicate that mitobronitol was less likely than phosphorus-32 or busulfan to induce acute myeloid leukaemia.

For a discussion of the usual management of polycythaemia vera, see p.654.

1. Kelemen E, *et al.* Decreasing risk of leukaemia during prolonged follow-up after mitobronitol therapy for polycythaemia vera. *Lancet* 1987; **ii:** 625.

Preparations

BP 2008: Mitobronitol Tablets.

Proprietary Preparations (details are given in Part 3)
Austria: Myelobromol; ***UK:*** Myelobromol.

Mitoguazone Dihydrochloride *(rINNM)*

Dihidrocloruro de mitoguazona; Methyl-GAG; Methylglyoxal Bisguanylhydrazone (mitoguazone); MGBG; Mitoguazone, Dichlorhydrate de; Mitoguazoni Dihydrochloridum; NSC-32946. 1,1′-[(Methylethanediylidene)dinitrilo]diguanidine dihydrochloride.

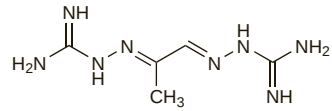
Митогуазона Дигидрохлорид

$C_5H_{12}N_8.2HCl$ = 257.1.

CAS — 459-86-9 (mitoguazone); 7059-23-6 (mitoguazone dihydrochloride).

ATC — L01XX16.

ATC Vet — QL01XX16.



(mitoguazone)

Profile

Mitoguazone is an antineoplastic that may exert its cytotoxic effects by its ability to inhibit polyamine biosynthesis. It has been tried as the dihydrochloride monohydrate or the acetate, in the treatment of leukaemias, lymphomas, and some solid tumours.

Mitoguazone may produce hypoglycaemia and should be given dissolved in glucose-containing infusion fluids; sugar may be taken orally if hypoglycaemia develops during infusion. Granulocytopenia and thrombocytopenia are generally mild and reversible on stopping treatment. Gastrointestinal effects frequently occur.

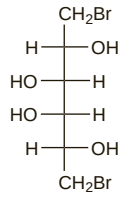
Mitolactol *(rINN)*

DBD; Dibromodulcitol; Mitolactolum; NSC-104800; WR-138743. 1,6-Dibromo-1,6-dideoxy-D-galactitol.

Митолактол

$C_6H_{12}Br_2O_4$ = 308.0.

CAS — 10318-26-0.



Profile

Mitolactol is an antineoplastic that may act by alkylation, probably as epoxide metabolites including dianhydrogalactitol. It has been given orally in the treatment of metastatic breast and cervi-

cal carcinoma, although other drugs are usually preferred, and has also been tried in other malignant neoplasms, notably those of the brain.

In addition to myelosuppression, which is usually dose-limiting, and manifests chiefly as leucopenia and thrombocytopenia, adverse effects include gastrointestinal disturbances, skin rashes, grey pigmentation of the skin, transient disturbances of hepatic function, elevated blood-urea nitrogen (BUN), and hypersensitivity reactions. Blood counts should be taken regularly during treatment and mitolactol withdrawn if bone-marrow depression occurs.

Mitomycin *(BAN, USAN, rINN)*

Mitomicina; Mitomicinas; Mitomicinum; Mitomisin; Mitomycin C; Mitomycine; Mitomycine C; Mitomycinum; Mitomysiini; NSC-26980. 6-Amino-1,1a,2,8,8a,8b-hexahydro-8-hydroxymethyl-8a-methoxy-5-methylazirino[2′,3′:3,4]pyrrolo[1,2-*a*]indole-4,7-dione carbamate; (1*S*,2*S*,9*S*,9a*R*)-7-Amino-2,3,5,8,9,9a-hexahydro-9a-methoxy-6-methyl-5,8-dioxo-1,2-epimino-1-*H*-pyrrolo[1,2-*a*]indol-9-ylmethyl carbamate.

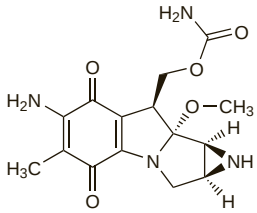
Митомицин

$C_{15}H_{18}N_4O_5$ = 334.3.

CAS — 50-07-7.

ATC — L01DC03.

ATC Vet — QL01DC03.



Description. Mitomycin is an antineoplastic antibiotic produced by the growth of *Streptomyces caespitosus*.

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

Ph. Eur. 6.2 (Mitomycin). A substance produced by a strain of *Streptomyces caespitotus*. Blue-violet crystals or crystalline powder. Slightly soluble in water and in acetone; freely soluble in dimethylacetamide; sparingly soluble in methyl alcohol. A 0.1% solution in water has a pH of 5.5 to 7.5. Protect from light.

USP 31 (Mitomycin). A blue-violet crystalline powder. It has a potency of not less than 970 micrograms/mg. Slightly soluble in water; soluble in acetone, in butyl acetate, in cyclohexanone, and in methyl alcohol. A 0.5% suspension in water has a pH of 6.0 to 7.5. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Incompatibility. Mitomycin may be incompatible with drugs that are acid in solution—for a report of incompatibility with topotecan, see p.780.

Stability. Mitomycin undergoes degradation in acid solution,[1] and two studies[2,3] suggested that mitomycin was much less stable in glucose 5% injection than in sodium chloride 0.9%. These findings were queried by a manufacturer (*Bristol, USA*) whose own results suggested[4] that mitomycin was stable for 48 hours in glucose injection 5% at 25°, and it is uncertain whether different manufacturers' formulations differ in stability, or, as has been suggested, that an unsuitable assay was used by the manufacturer to measure stability.[5]

1. Beijnen JH, Underberg WJM. Degradation of mitomycin C in acidic solution. *Int J Pharmaceutics* 1985; **24:** 219–29.
2. Benvenuto JA, *et al.* Stability and compatibility of antitumour agents in glass and plastic containers. *Am J Hosp Pharm* 1981; **38:** 1914–18.
3. Quebbeman EJ, *et al.* Stability of mitomycin admixtures. *Am J Hosp Pharm* 1985; **42:** 1750–4.
4. Keller JH. Stability of mitomycin admixtures. *Am J Hosp Pharm* 1986; **43:** 59,64.
5. Quebbeman EJ, Hoffman NE. Stability of mitomycin admixtures. *Am J Hosp Pharm* 1986; **43:** 64.

Adverse Effects, Treatment, and Precautions

For general discussions see Antineoplastics, p.635, p.639, and p.641.

The main adverse effect of mitomycin is delayed cumulative bone-marrow suppression. Profound leucopenia and thrombocytopenia occurs after about 4 weeks with recovery in about 8 to 10 weeks after a dose. Blood counts may not recover in about one-quarter of patients. Other serious adverse effects include renal damage and pulmonary reactions; a potentially fatal haemolytic-uraemic syndrome has been reported in some patients. US licensed product information states that the degree of renal impairment does not appear to be related to dose or duration of therapy although it has been suggested that the incidence of renal toxicity is greatly increased if the total cumulative dose exceeds 120 mg (see also Effects on the Kidneys, below). Gastrointestinal toxicity, dermatitis, alopecia, fever, malaise, and rarely cardiotoxicity may also occur. Local tissue necrosis, ulceration, and cellulitis may follow extravasation.

Mitomycin is contra-indicated in patients with impaired renal function or coagulation disorders. Renal function should be tested before beginning treatment and after each course.

Effects on the bladder. Intravesical instillation of mitomycin after resection of superficial bladder tumours has led to the development of indolent asymptomatic ulcers at the resection site which may persist for months, and must be distinguished from persistent infiltrating bladder cancer.[1,2] Persistent ulceration, inflammation, necrosis, and pain has also occurred, possibly because of mitomycin extravasation at the resection site.[3] There are also a few reports[4] of eosinophilic cystitis, in which eosinophilic infiltration of the mucosa and muscle were accompanied by oedema, inflammation, muscle necrosis and fibrosis. Severe bladder contracture is a rare, and often irreversible, complication of intravesical mitomycin;[5] urinary diversion may be required in cases of intolerable urinary frequency.[6] Formation of papillary-like calcifications at the resection site,[7] and calcification of the bladder wall have also been described after the use of mitomycin for superficial transitional cell carcinoma of the bladder.

See also under Effects on the Skin, below.

1. Richards B, Tolley D. Benign ulcers after bladder instillation of mitomycin C. *Lancet* 1986; **i:** 45.
2. Hetherington JW, Whelan P. Persistent ulcers after bladder instillation of mitomycin C. *Lancet* 1986; **i:** 324.
3. Cliff AM, *et al.* Perivesical inflammation after early mitomycin C instillation. *BJU Int* 2000; **85:** 556–7.
4. Ülker V, *et al.* Eosinophilic cystitis induced by mitomycin-C. *Int Urol Nephrol* 1996; **28:** 755–9.
5. Punga-Maole ML, *et al.* Rétraction vésicale, complication de la chimioprophylaxie du cancer vésical superficiel par mitomycine C endovésicale: a propos d'un cas et revue de la littérature. *Prog Urol* 1995; **5:** 580–5.
6. Wajsman Z, *et al.* Severely contracted bladder following intravesical mitomycin C therapy. *J Urol (Baltimore)* 1983; **130:** 340–1.
7. Fiore AA, *et al.* Papillary-like bladder calcifications following intravesical mitomycin C: a case report. *Minerva Urol Nefrol* 1993; **45:** 171–3.

Effects on the eyes. Early complications after the topical use of mitomycin with glaucoma filtering surgery (see Glaucoma, below) include hypotony, shallow anterior chamber, cataract formation, choroidal effusions, hypotonous maculopathy, and suprachoroidal haemorrhage.[1] Late complications include bleb leak, blebitis, and endophthalmitis.[2] Complications from the topical use of mitomycin with or after pterygium surgery (see Pterygium, below) commonly include irritation and photophobia. Other effects include delayed epithelial healing, avascularity of the sclera and cornea, scleral calcification and ulceration, necrotising scleritis, corneal or scleral perforation, iridocyclitis, cataract formation, glaucoma, and symblepharon.[1] Some of these effects may be severe and sight-threatening, and require further surgery.[3] Complications most commonly reported after the use of topical mitomycin in ocular surface neoplasia were hypersensitivity reactions and epiphora (an overflow of tears) secondary to stenosis of the lachrymal punctum.[4]

1. Hardten DR, Samuelson TW. Ocular toxicity of mitomycin-C. *Int Ophthalmol Clin* 1999; **39:** 79–90.
2. DeBry PW, *et al.* Incidence of late-onset bleb-related complications following trabeculectomy with mitomycin. *Arch Ophthalmol* 2002; **120:** 297–300.
3. Rubinfeld RS, *et al.* Serious complications of topical mitomycin C after pterygium surgery. *Ophthalmology* 1992; **99:** 1647–54.
4. Khong JJ, Muecke J. Complications of mitomycin C therapy in 100 eyes with ocular surface neoplasia. *Br J Ophthalmol* 2006; **90:** 819–22.

Effects on the kidneys. A syndrome of thrombotic microangiopathy resembling the haemolytic-uraemic syndrome has been seen in patients receiving mitomycin, either alone[1] or more often with other drugs, particularly fluorouracil[2] or tamoxifen.[3,4] The syndrome is characterised by haemolytic anaemia, thrombocytopenia, and progressive renal failure, and may be accompanied by hypertension, pulmonary oedema, and neurological effects including confusion, headache, and seizures.[1,2] Onset is usually delayed, sometimes occurring several months after the end of a course of mitomycin.[1,2]

There is some uncertainty as to whether mitomycin dose is significant, but one study[1] found that all of 25 cases they reported had received total doses of 70 mg or more, and another[2] reported that 74 of 83 cases had received 60 mg or more.

Symptoms may be exacerbated by blood transfusions.[2] The use of erythropoietin allowed the cessation of blood transfusion, with subsequent haematological improvement and slower progression of chronic renal failure in one case report.[5] Plasma exchange has been suggested as possibly helpful,[1] although only a minority of patients may benefit from this treatment.[2] Captopril therapy may also be useful.[6]

1. Cordonnier D, *et al.* La néphrotoxicité de la mitomycine C (à propos de 25 observations): résultats d'une enquête multicentrique organisée par la société de néphrologie. *Nephrologie* 1985; **6:** 19–26.
2. Lesesne JB, *et al.* Cancer-associated hemolytic-uremic syndrome: analysis of 85 cases from a national registry. *J Clin Oncol* 1989; **7:** 781–9.
3. Montes A, *et al.* A toxic interaction between mitomycin C and tamoxifen causing the haemolytic uraemic syndrome. *Eur J Cancer* 1993; **29**A: 1854–7.
4. Ellis PA, *et al.* Haemolytic uraemic syndrome in a patient with lung cancer: further evidence for a toxic interaction between mitomycin-C and tamoxifen. *Clin Oncol (R Coll Radiol)* 1996; **8:** 402–3.
5. Catalano C, *et al.* Erythropoietin is beneficial in mitomycin-induced hemolytic-uremic syndrome. *Nephron* 2002; **91:** 324–6.
6. Schiebe ME, *et al.* Mitomycin C-related hemolytic uremic syndrome in cancer patients. *Anticancer Drugs* 1998; **9:** 433–5.

Effects on the liver. Hepatic veno-occlusive disease developed in 6 of 29 patients given intensive mitomycin therapy and autologous bone marrow transplantation.[1] The effect was manifest as abdominal pain, hepatomegaly, and ascites, and liver failure was progressive and fatal in 3. A further patient, who had no symptoms, was found to have veno-occlusive disease at post mortem.

1. Lazarus HM, *et al.* Veno-occlusive disease of the liver after high-dose mitomycin C therapy and autologous bone marrow transplantation. *Cancer* 1982; **49:** 1789–95.

Effects on respiratory function. Mitomycin-induced pulmonary toxicity has been reviewed.[1,2] There have been reports of toxicity at total dosages as low as 20 mg/m^2 of mitomycin,[2] although others report[1] that the average cumulative dose associated with toxicity is 78 mg. Premedication with corticosteroids may reduce the incidence of lung toxicity.[2]

See also Effects on the Lungs, p.638. For reference to the respiratory effects of mitomycin used with a vinca alkaloid see Interactions, Antineoplastics, under Vinblastine Sulfate, p.786.

1. Linette DC, *et al.* Mitomycin-induced pulmonary toxicity: case report and review of the literature. *Ann Pharmacother* 1992; **26:** 481–4.
2. Okuno SH, Frytak S. Mitomycin lung toxicity: acute and chronic phases. *Am J Clin Oncol* 1997; **20:** 282–4.

Effects on the skin. Severe eczema of the hands and feet and generalised rash have been reported in patients receiving intravesical mitomycin.[1,2] These symptoms appear to be due to a delayed hypersensitivity (type IV) reaction,[1,2] which is probably also responsible for the bladder irritation and cystitis that may follow intravesical mitomycin[1] (see above). Leucocytoclastic vasculitis caused by an immune-complex mediated (type III) reaction and presenting as purpuric papules has also been described.[2]

1. Colver GB, *et al.* Dermatitis due to intravesical mitomycin C: a delayed-type hypersensitivity reaction? *Br J Dermatol* 1990; **122:** 217–24.
2. Kunkeler L, *et al.* Type III and type IV hypersensitivity reactions due to mitomycin C. *Contact Dermatitis* 2000; **42:** 74–6.

Interactions

For a general outline of antineoplastic drug interactions, see p.642.

Antineoplastics. Cardiotoxicity developed in 14 of 91 patients who received mitomycin therapy as second-line treatment for breast cancer after the failure of *doxorubicin*-containing regimens, compared with 3 of 89 similar patients whose second-line treatment did not include mitomycin.[1]

For reports of acute bronchospasm after injection of a *vinca alkaloid* in patients pretreated with mitomycin see Vinblastine Sulfate, p.786. For the increased risk of haemolytic-uraemic syndrome that may occur if mitomycin is given with *fluorouracil* or *tamoxifen* see under Effects on the Kidneys, above.

1. Buzdar AU, *et al.* Adriamycin and mitomycin C: possible synergistic cardiotoxicity. *Cancer Treat Rep* 1978; **62:** 1005–8.

Pharmacokinetics

Mitomycin disappears rapidly from the blood after intravenous injection with an initial (distribution) half-life of 17 minutes. It is widely distributed but does not appear to cross the blood-brain barrier. Mitomycin is metabolised mainly but not exclusively in the liver. The terminal half-life is about 50 minutes. After normal doses about 10% of a dose is excreted unchanged in the urine; small amounts are also present in bile and faeces. With increasing doses metabolic pathways are saturated, and more drug is excreted unchanged in the urine.

Uses and Administration

Mitomycin is a highly toxic antibiotic with antineoplastic properties. It acts as an alkylating agent after activation *in vivo* and suppresses the synthesis of nucleic acids. It is a cell-cycle non-specific agent, but is most active in the late G_1 and early S phases.