some of which have oestrogen antagonist activity, and is excreted in the faeces. After intramuscular injection fulvestrant has a half-life of about 40 to 50 days.

◊ References.

1. Robertson JFR, *et al.* Pharmacokinetic profile of intramuscular fulvestrant in advanced breast cancer. *Clin Pharmacokinet* 2004; **43:** 529–38.

Uses and Administration

Fulvestrant is an oestrogen antagonist that downregulates the oestrogen receptor and is used for the treatment of oestrogen-receptor positive, locally advanced or metastatic breast cancer in postmenopausal women (p.661); it is given when disease has relapsed or progressed during or after treatment with anti-oestrogens. The recommended dose is 250 mg, given intramuscularly at monthly intervals. It is injected into the buttock, either as a single injection or as two concurrent doses.

◊ References.

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3. Bross PF, *et al.* Fulvestrant in postmenopausal women with advanced breast cancer. *Clin Cancer Res* 2003; **9:** 4309–17.
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9. Bundred N. Preclinical and clinical experience with fulvestrant (Faslodex) in postmenopausal women with hormone receptor-positive advanced breast cancer. *Cancer Invest* 2005; **23:** 173–81.
10. Buzdar AU, Robertson JFR. Fulvestrant: pharmacologic profile versus existing endocrine agents for the treatment of breast cancer. *Ann Pharmacother* 2006; **40:** 1572–83.

Preparations

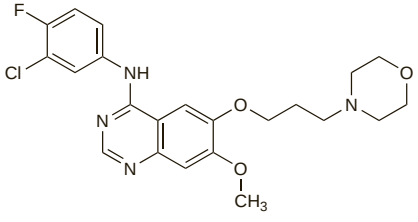
Proprietary Preparations (details are given in Part 3)
Arg.: Faslodex; ***Austral.:*** Faslodex; ***Belg.:*** Faslodex; ***Braz.:*** Faslodex; ***Canad.:*** Faslodex; ***Cz.:*** Faslodex; ***Denm.:*** Faslodex; ***Fin.:*** Faslodex; ***Fr.:*** Faslodex; ***Ger.:*** Faslodex; ***Gr.:*** Faslodex; ***Hung.:*** Faslodex; ***Irl.:*** Faslodex; ***Israel:*** Faslodex; ***Ital.:*** Faslodex; ***Malaysia:*** Faslodex; ***Mex.:*** Faslodex; ***Neth.:*** Faslodex; ***Norw.:*** Faslodex; ***NZ:*** Faslodex; ***Pol.:*** Faslodex; ***Port.:*** Faslodex; ***Rus.:*** Faslodex (Фазлодекс); ***Spain:*** Faslodex; ***Swed.:*** Faslodex; ***Switz.:*** Faslodex; ***UK:*** Faslodex; ***USA:*** Faslodex; ***Venez.:*** Faslodex.

Gefitinib *(BAN, USAN, rINN)*

Géfitinib; Gefitinibum; ZD-1839. *N*-(3-Chloro-4-fluorophenyl)-7-methoxy-6-[3-(morpholin-4-yl)propoxy]quinazolin-4-amine.

Гефитиниб

$C_{22}H_{24}ClFN_4O_3$ = 446.9.
CAS — 184475-35-2.
ATC — L01XE02.
ATC Vet — QL01XE02.



Profile

Gefitinib is a selective inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor. It blocks signal transduction pathways implicated in the growth of tumour cells. It is given orally for the management of locally advanced or metastatic non-small cell lung cancer (p.668) unresponsive to other therapy; the usual dose is 250 mg daily. In the USA, use is restricted to those patients who are currently receiving and benefiting from gefitinib, or to those who have previously benefited from therapy. Adverse effects include rashes and diarrhoea. There have been reports of severe diffuse parenchymal lung disease, including fatalities. There are also reports of tumour haemorrhage, sometimes fatal, after use of gefitinib in patients with head and neck cancer. Gefitinib is under investigation in the management of other solid tumours.

◊ References.

1. Culy CR, Faulds D. Gefitinib. *Drugs* 2002; **62:** 2237–48.
2. Inoue A, *et al.* Severe acute interstitial pneumonia and gefitinib. *Lancet* 2003; **361:** 137–9.
3. Kris MG, *et al.* Efficacy of gefitinib, an inhibitor of the epidermal growth factor receptor tyrosine kinase, in symptomatic patients with non–small cell lung cancer: a randomized trial. *JAMA* 2003; **290:** 2149–58.
4. Liu CY, Seen S. Gefitinib therapy for advanced non–small-cell lung cancer. *Ann Pharmacother* 2003; **37:** 1644–53.
5. Cersosimo RJ. Gefitinib: a new antineoplastic for advanced non-small-cell lung cancer. *Am J Health-Syst Pharm* 2004; **61:** 889–98.
6. Forsythe B, Faulkner K. Overview of the tolerability of gefitinib (IRESSA) monotherapy: clinical experience in non-small-cell lung cancer. *Drug Safety* 2004; **27:** 1081–92.
7. Frampton JE, Easthope SE. Gefitinib: a review of its use in the management of advanced non-small-cell lung cancer. *Drugs* 2004; **64:** 2475–92.
8. Tanovic A, Alfaro V. Gefitinib: current status in the treatment of non-small cell lung cancer. *Drugs Today* 2004; **40:** 809–27.
9. Birnbaum A, Ready N. Gefitinib therapy for non-small cell lung cancer. *Curr Treat Options Oncol* 2005; **6:** 75–81.
10. Shah NT, *et al.* Practical management of patients with non-small-cell lung cancer treated with gefitinib. *J Clin Oncol* 2005; **23:** 165–74.
11. Swaisland HC, *et al.* Pharmacokinetic drug interactions of gefitinib with rifampicin, itraconazole and metoprolol. *Clin Pharmacokinet* 2005; **44:** 1067–81.
12. Swaisland HC, *et al.* Single-dose clinical pharmacokinetic studies of gefitinib. *Clin Pharmacokinet* 2005; **44:** 1165–77.
13. Blackhall F, *et al.* Where next for gefitinib in patients with lung cancer? *Lancet Oncol* 2006; **7:** 499–507.

Effects on survival. In chemotherapy-naive patients with advanced non-small cell lung cancer, gefitinib, given with gemcitabine plus cisplatin,[1] or paclitaxel plus carboplatin,[2] showed no survival advantage over chemotherapy without gefitinib. In a large study in patients with non-small cell lung cancer given gefitinib or placebo, after failure of one or two previous treatment regimens, no survival benefit was shown with gefitinib;[3] recommendations restricting the use of gefitinib to selected patients have been made in the USA (see above).[4] However, a subset analysis of study data found an improvement in survival in a subgroup of patients of Asian origin.[5] In reports of the IMEX study in patients with head and neck cancer, no survival advantage for gefitinib was found when compared with methotrexate; an increased incidence of tumour haemorrhage was seen in those treated with gefitinib.[6] Studies have suggested that there are subgroups of patients with non-small cell lung cancer who have specific biomarkers or mutations in the epidermal growth factor receptor gene which correlate with clinical response to gefitinib.[7-10]

A small retrospective study found that further treatment with gefitinib prolonged survival in patients who were initially responsive, but who had subsequent disease progression upon stopping therapy.[11]

1. Giaccone G, *et al.* Gefitinib in combination with gemcitabine and cisplatin in advanced non–small-cell lung cancer: a phase III trial—INTACT 1. *J Clin Oncol* 2004; **22:** 777–84.
2. Herbst RS, *et al.* Gefitinib in combination with paclitaxel and carboplatin in advanced non–small-cell lung cancer: a phase III trial—INTACT 2. *J Clin Oncol* 2004; **22:** 785–94.
3. Thatcher N, *et al.* Gefitinib plus best supportive care in previously treated patients with refractory advanced non-small-cell lung cancer: results from a randomised, placebo-controlled, multicentre study (Iressa Survival Evaluation in Lung Cancer). *Lancet* 2005; **366:** 1527–37.
4. FDA Public Health Advisory. New labeling and distribution program for gefitinib (Iressa) (issued 17/06/05). Available at: http://www.fda.gov/cder/drug/advisory/iressa.htm (accessed 13/03/06)
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6. AstraZeneca, Canada. Health Canada endorsed important safety information on Iressa (gefitinib): lack of survival benefit and increased incidence of tumour haemorrhage in association with IRESSA in patients with squamous cell carcinoma of the head and neck (SCCHN) (issued 1st December 2006). Available at: http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2006/iressa_4_hpc-cps-eng.php (accessed 01/08/08)
7. Lynch TJ, *et al.* Activating mutations in the epidermal growth factor receptor underlying responsiveness of non–small-cell lung cancer to gefitinib. *N Engl J Med* 2004; **350:** 2129–39.
8. Paez JG, *et al.* EGFR mutations in lung cancer: correlation with clinical response to gefitinib therapy. *Science* 2004; **304:** 1497–1500.
9. Pao W, Miller VA. Epidermal growth factor receptor mutations, small-molecule kinase inhibitors, and non–small-cell lung cancer: current knowledge and future directions. *J Clin Oncol* 2005; **23:** 2556–68.
10. Hirsch FR, *et al.* Molecular predictors of outcome with gefitinib in a phase III placebo-controlled study in advanced non-small-cell lung cancer. *J Clin Oncol* 2006; **24:** 5034–42.
11. Yokouchi H, *et al.* Clinical benefit of readministration of gefitinib for initial gefitinib-responders with non-small cell lung cancer. *BMC Cancer* 2007; **7:** 51.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Iressa; ***Austral.:*** Iressa; ***Canad.:*** Iressa; ***Chile:*** Iressa; ***Fr.:*** Iressa†; ***Hong Kong:*** Iressa; ***India:*** Geftinat; ***Indon.:*** Iressa; ***Israel:*** Iressa; ***Malaysia:*** Iressa; ***Mex.:*** Iressa; ***NZ:*** Iressa; ***Philipp.:*** Iressa; ***Rus.:*** Iressa (Иресса); ***Singapore:*** Iressa; ***Switz.:*** Iressa; ***Thai.:*** Iressa; ***UK:*** Iressa; ***USA:*** Iressa; ***Venez.:*** Iressa.

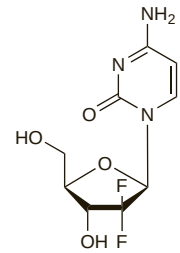
Gemcitabine Hydrochloride

(BANM, USAN, rINNM)

Gemcitabine, chlorhydrate de; Gemcitabini hydrochloridum; Hidrocloruro de gemcitabina; LY-188011 (gemcitabine). 4-Amino-1-(2-deoxy-2,2-difluoro-β-D-ribofuranosyl)pyrimidin-2(1*H*)-one hydrochloride; 2′-Deoxy-2′,2′-difluorocytidine hydrochloride.

Гемцитабина Гидрохлорид

$C_9H_{11}F_2N_3O_4$,HCl = 299.7.
CAS — 95058-81-4 (gemcitabine); 122111-03-9 (gemcitabine hydrochloride).
ATC — L01BC05.
ATC Vet — QL01BC05.



(gemcitabine)

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

Ph. Eur. 6.2 (Gemcitabine Hydrochloride). A white or almost white powder. Soluble in water; slightly soluble in methyl alcohol; practically insoluble in acetone. A 1% solution in water has a pH of 2.0 to 3.0.

USP 31 (Gemcitabine Hydrochloride). A white to off-white solid. Soluble in water; practically insoluble in alcohol and in polar organic solvents; slightly soluble in methyl alcohol. pH of a 1% solution in water is between 2.0 and 3.0. Store in airtight containers.

Incompatibility. Gemcitabine hydrochloride was reported to be physically incompatible with aciclovir sodium, amphotericin B, cefoperazone sodium, cefotaxime sodium, furosemide, ganciclovir sodium, imipenem with cilastatin sodium, irinotecan, methotrexate sodium, methylprednisolone sodium succinate, mezlocillin sodium, mitomycin, piperacillin sodium, piperacillin sodium with tazobactam, and prochlorperazine edisilate during simulated Y-site administration.[1]

1. Trissel LA, *et al.* Compatibility of gemcitabine hydrochloride with 107 selected drugs during simulated Y-site injection. *J Am Pharm Assoc* 1999; **39:** 514–18.

Adverse Effects, Treatment, and Precautions

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

The major dose-limiting adverse effect of gemcitabine is bone-marrow depression, although this is reported to be modest and rarely requires stopping therapy. Gastrointestinal disturbances occur, especially nausea and vomiting, but these are usually of mild to moderate severity. Rashes, often associated with pruritus, and flu-like symptoms are relatively common. Oedema, dyspnoea, and alopecia are also commonly reported. Pulmonary oedema has been reported infrequently; interstitial pneumonitis, pulmonary fibrosis, and acute respiratory distress syndrome have occurred. Therapy should be stopped if pulmonary toxicity occurs. There are rare cases of hypotension, anaphylactoid reactions, and severe desquamative and bullous skin eruptions. Haematuria, proteinuria, transient liver enzyme elevations, and serious hepatotoxicity, including liver failure and death, have been reported. It should therefore be used with caution in patients with impaired renal or hepatic function. Haemolytic-uraemic syndrome and/or thrombocytopenic purpura have been reported and have led to irreversible renal failure; gemcitabine

should be stopped at the first signs of microangiopathic haemolytic anaemia. Congestive heart failure, myocardial infarction, or arrhythmias may occur rarely.

Gemcitabine may produce somnolence: patients so affected should not drive or operate machinery. Severe toxicity, in the form of potentially life-threatening oesophagitis and pneumonitis has been seen in patients given radical radiotherapy to the thorax concurrently with gemcitabine.

Effects on the nervous system. A report of autonomic neuropathy associated with gemcitabine therapy.[1] Symptoms resolved 4 weeks after stopping therapy.

1. Dormann AJ, *et al.* Gemcitabine-associated autonomic neuropathy. *Lancet* 1998; **351:** 644.

Effects on the skin. A patient who received gemcitabine 1 week after having had phototherapy developed a severe sunburn reaction in those areas exposed to UVB. The erythema resolved spontaneously, but recurred with each subsequent dose of gemcitabine, and became progressively more intense. A short course of high-dose prednisone was given with topical triamcinolone, and the patient was safely rechallenged with 2 further doses of gemcitabine.[1]

1. Badger J, *et al.* Photo therapy recall with gemcitabine following ultraviolet B treatment. *J Clin Oncol* 2005; **23:** 7224–5.

Peripheral ischaemia. Pain, coldness, colour changes, and distal claudication in the feet have been reported in patients treated with gemcitabine and cisplatin.[1] Pain and colour changes in the fingertips have also been reported after gemcitabine monotherapy.[2]

1. Barceló R, *et al.* Distal ischemic changes related to combination chemotherapy with cisplatin and gemcitabine: description of four cases. *Ann Oncol* 2000; **11:** 1191–4.
2. Yildiz R, *et al.* Digital ischemic changes after gemcitabine therapy in a patient with metastatic non-small-cell lung cancer. *Ann Pharmacother* 2007; **41:** 901–2.

Interactions

Antineoplastics. In a study[1] of 14 patients with lung cancer, the use of *paclitaxel* before gemcitabine caused a decrease in the systemic clearance, volume of distribution, and interpatient pharmacokinetic variability of gemcitabine. This resulted in plasma concentrations of gemcitabine slightly higher than the desired range. However, there was no apparent relationship between pharmacokinetic changes and toxicity, and the clinical significance of this possible interaction is unclear.

A trial investigating a modified chemotherapy regimen in which gemcitabine was substituted for etoposide was stopped because of unexpected pulmonary toxicity. This was considered to be due to the combination of gemcitabine and *bleomycin*, as the adverse effect was apparent in other studies using this combination.[2]

1. Shord SS, *et al.* Gemcitabine pharmacokinetics and interaction with paclitaxel in patients with advanced non-small-cell lung cancer. *Cancer Chemother Pharmacol* 2003; **51:** 328–36.
2. Bredenfeld H, *et al.* Severe pulmonary toxicity in patients with advanced-stage Hodgkin's disease treated with a modified bleomycin, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone, and gemcitabine (BEACOPP) regimen is probably related to the combination of gemcitabine and bleomycin: a report of the German Hodgkin's lymphoma study group. *J Clin Oncol* 2004; **22:** 2424–9.

Pharmacokinetics

After intravenous doses gemcitabine is rapidly cleared from the blood and metabolised by cytidine deaminase in the liver, kidney, blood, and other tissues. Clearance is about 25% lower in women than in men. Almost all of the dose is excreted in urine as 2′-deoxy-2′,2′-difluorouridine (dFdU), only about 1% being found in the faeces. Intracellular metabolism produces mono-, di-, and triphosphate metabolites, the latter two active. The half-life of gemcitabine ranges from 42 to 94 minutes depending on age and gender. The intracellular half-life of the triphosphate is stated to range from 0.7 to 12 hours.

◊ References.

1. Johnson SA. Clinical pharmacokinetics of nucleoside analogues: focus on haematological malignancies. *Clin Pharmacokinet* 2000; **39:** 5–26.
2. Shamseddine AI, *et al.* Comparative pharmacokinetics and metabolic pathway of gemcitabine during intravenous and intra-arterial delivery in unresectable pancreatic cancer patients. *Clin Pharmacokinet* 2005; **44:** 957–67.

Uses and Administration

Gemcitabine is an analogue of cytarabine (p.705) that is metabolised intracellularly to active diphosphate and triphosphate nucleosides, which inhibit DNA synthesis and induce apoptosis. It is primarily active against cells in S phase. It is given in the management of solid tumours including those of the bladder, breast, lung, ovary, and pancreas (see p.659, p.661, p.668, p.670, and p.671, respectively).

Gemcitabine is given intravenously as the hydrochloride. Doses are calculated in terms of the base; gemcitabine hydrochloride 1.14 g is equivalent to about 1 g of gemcitabine. Doses are reconstituted in sodium chloride 0.9%. The concentration of the infusion solution should not exceed the equivalent of gemcitabine 40 mg/mL. Gemcitabine is given by infusion over 30 to 60 minutes; doses are subsequently adjusted according to response and toxicity.

In the treatment of **pancreatic cancer**, an initial course of gemcitabine 1 g/m^2 once weekly for up to 7 weeks may be given, followed after a one-week recovery period by a regimen of infusions once weekly for 3 consecutive weeks out of 4.

In **non-small cell lung cancer**, gemcitabine may be given as a single agent; 1 g/m^2 once weekly for 3 consecutive weeks out of 4 is recommended. Alternatively, it may be given before cisplatin. Two schedules have been used; gemcitabine 1.25 g/m^2 is given on days 1 and 8 of a 21-day cycle, or gemcitabine 1 g/m^2 is given on days 1, 8 and 15 of a 28-day cycle.

In the treatment of **bladder cancer**, gemcitabine is given before cisplatin. The recommended dose of gemcitabine is 1 g/m^2 on days 1, 8, and 15 of a 28-day cycle.

In **breast cancer**, gemcitabine is usually given after a taxane such as paclitaxel. A dose of gemcitabine 1.25 g/m^2 is given on days 1 and 8 of a 21-day cycle.

In **ovarian cancer**, gemcitabine is given before carboplatin. The recommended dose of gemcitabine is 1 g/m^2 on days 1 and 8 of a 21-day cycle.

◊ References.

1. Stadler WM. Gemcitabine doublets in advanced urothelial cancer. *Semin Oncol* 2002; **29** (suppl 3): 15–19.
2. Hussain M, *et al.* Novel gemcitabine-containing triplets in the management of urothelial cancer. *Semin Oncol* 2002; **29** (suppl 3): 20–4.
3. Hochster HS. Newer approaches to gemcitabine-based therapy of pancreatic cancer: fixed-dose-rate infusion and novel agents. *Int J Radiat Oncol Biol Phys* 2003; **56** (suppl): 24–30.
4. Yardley DA. Gemcitabine and taxanes as a new standard of care in breast cancer. *Clin Breast Cancer* 2004; **4** (suppl 3): S107–S112.
5. Natale R. A ten-year review of progress in the treatment of non-small-cell lung cancer with gemcitabine. *Lung Cancer* 2005; **50** (suppl): S2–S4.
6. Saha A, Rudd R. Gemcitabine and carboplatin: is this the best combination for non-small cell lung cancer? *Expert Rev Anticancer Ther* 2006; **6:** 165–73.
7. Kose MF, *et al.* Gemcitabine plus carboplatin in platinum-sensitive recurrent ovarian carcinoma. *Expert Rev Anticancer Ther* 2006; **6:** 437–43.
8. Wirk B, Perez E. Role of gemcitabine in breast cancer management: an update. *Semin Oncol* 2006; **33** (suppl 2): S6–S14.
9. Pfisterer J, *et al.* Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: an intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG. *J Clin Oncol* 2006; **24:** 4699–4707.
10. Kiba T, *et al.* Single-agent gemcitabine for biliary tract cancers: study outcomes and systematic review of the literature. *Oncology* 2006; **70:** 358–65.
11. Maki RG. Gemcitabine and docetaxel in metastatic sarcoma: past, present, and future. *Oncologist* 2007; **12:** 999–1006.
12. El Karak F, Flechon A. Gemcitabine in bladder cancer. *Expert Opin Pharmacother* 2007; **8:** 3251–6.
13. Serrano A, Gerson R. Chemotherapy with gemcitabine in advanced biliary tract carcinoma. *Rev Recent Clin Trials* 2008; **3:** 70–8.
14. Hilbig A, Oettle H. Gemcitabine in the treatment of metastatic pancreatic cancer. *Expert Rev Anticancer Ther* 2008; **8:** 511–23.
15. Dent S, *et al.* Gemcitabine in the management of metastatic breast cancer: a systematic review. *Breast Cancer Res Treat* 2008; **108:** 319–31.

Preparations

USP 31: Gemcitabine for Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Abine; Antoril; Eriogem; Gemtro; Gezt; Gramagen; ***Austral.:*** Gemzar; ***Austria:*** Gemzar; ***Belg.:*** Gemzar; ***Braz.:*** Gemzar; ***Canad.:*** Gemzar; ***Chile:*** Gemzar; ***Cz.:*** Gemzar; ***Denm.:*** Gemzar; ***Fin.:*** Gemzar; ***Fr.:*** Gemzar; ***Ger.:*** Gemzar; ***Gr.:*** Gemzar; ***Hong Kong:*** Gemzar; ***Hung.:*** Gemzar; ***India:*** Gemcite; Oncogem; ***Indon.:*** Gemzar; ***Irl.:*** Gemzar; ***Israel:*** Gemzar; ***Ital.:*** Gemzar; ***Malaysia:*** Gemzar; ***Mex.:*** Gemzar; ***Neth.:*** Gemzar; ***Norw.:*** Gemzar; ***NZ:*** Gemzar; ***Philipp.:*** Gemzar; ***Pol.:*** Gemzar; ***Port.:*** Gemzar; ***Rus.:*** Gemzar (Гемзар); ***S.Afr.:*** Gemzar; ***Singapore:*** Gemzar; ***Spain:*** Gemzar; ***Swed.:*** Gemzar; ***Switz.:*** Gemzar; ***Thai.:*** Gemzar; ***Turk.:*** Gemzar; ***UK:*** Gemzar; ***USA:*** Gemzar; ***Venez.:*** Gemzar.

Gemtuzumab Ozogamicin *(USAN, rINNM)*

CDP-771; CMA-676; Gemtuzumab ozogamicina; Gemtuzumab Ozogamicine; Gemtuzumab Zogamicin; Gemtuzumabum Ozogamicinum; WAY-CMA-676. Immunoglobulin G4 (human-mouse monoclonal hP67.6 κ4-chain anti-human antigen CD 33), disulfide with human-mouse monoclonal hP67.6 κ-chain, dimer conjugate with ozogamicin.

Гемтузумаб Озогамицин

CAS — 220578-59-6.
ATC — L01XC05.
ATC Vet — QL01XC05.

Adverse Effects and Precautions

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

Myelosuppression is common with gemtuzumab ozogamicin, and thrombocytopenia may be prolonged. Infusion-related reactions characteristic of a cytokine release syndrome (including fever, chills, dyspnoea, and hypotension) and hypersensitivity may occur; prophylactic use of an antihistamine and paracetamol is recommended. Pulmonary sequelae may be fatal. Hepatotoxicity, including severe veno-occlusive disease, has also been reported. Electrolyte imbalances, especially hypokalaemia and hypomagnesaemia, and gastrointestinal disturbances may occur.

Blood and platelet counts, electrolytes, and liver function tests should be regularly monitored.

Hypersensitivity. A 75-year-old man with acute myeloid leukaemia developed severe respiratory distress and died after being given gemtuzumab ozogamicin and platelets on the same day. He had previously had the drug and platelets on separate occasions with no untoward effects. It was suggested that this combination contributed to a fatal hypersensitivity reaction.[1]

1. Hanbali A, *et al.* Fatal hypersensitivity reaction to gemtuzumab ozogamicin associated with platelet transfusion. *Am J Health-Syst Pharm* 2007; **64:** 1401–2.

Uses and Administration

Gemtuzumab ozogamicin is a recombinant humanised monoclonal antibody conjugated with calicheamicin, a cytotoxic antibiotic. The antibody binds specifically to the CD33 antigen, which is expressed on leukaemic myeloblasts but not normal haematopoietic stem cells. Gemtuzumab ozogamicin is licensed for the second-line treatment of CD33-positive acute myeloid leukaemia (p.652) in elderly patients who are unable to tolerate conventional chemotherapy. It is given in 100 mL of sodium chloride 0.9% via an in-line 1.2 micron filter. The licensed dose is 9 mg/m^2 given by intravenous infusion over 2 hours, repeated once after 14 days. Lower doses are under investigation as part of combined induction or consolidation regimens.

◊ References.

1. McGavin JK, Spencer CM. Gemtuzumab ozogamicin. *Drugs* 2001; **61:** 1317–22.
2. Dowell JA, *et al.* Pharmacokinetics of gemtuzumab ozogamicin, an antibody-targeted chemotherapy agent for the treatment of patients with acute myeloid leukemia in first relapse. *J Clin Pharmacol* 2001; **41:** 1206–14.
3. Sievers EL, *et al.* Efficacy and safety of gemtuzumab ozogamicin in patients with CD33-positive acute myeloid leukemia in first relapse. *J Clin Oncol* 2001; **19:** 3244–54.
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5. Larson RA, *et al.* Antibody-targeted chemotherapy of older patients with acute myeloid leukemia in first relapse using Mylotarg (gemtuzumab ozogamicin). *Leukemia* 2002; **16:** 1627–36.
6. Buckwalter M, *et al.* Pharmacokinetics of gemtuzumab ozogamicin as a single-agent treatment of pediatric patients with refractory or relapsed acute myeloid leukemia. *J Clin Pharmacol* 2004; **44:** 873–80.
7. Lo-Coco F, *et al.* Gemtuzumab ozogamicin (Mylotarg) as a single agent for molecularly relapsed acute promyelocytic leukemia. *Blood* 2004; **104:** 1995–9.
8. Fenton C, Perry CM. Gemtuzumab ozogamicin: a review of its use in acute myeloid leukaemia. *Drugs* 2005; **65:** 2405–27.
9. Tsimberidou AM, *et al.* The role of gemtuzumab ozogamicin in acute leukaemia therapy. *Br J Haematol* 2006; **132:** 398–409.
10. Stasi R, *et al.* Gemtuzumab ozogamicin in the treatment of acute myeloid leukemia. *Cancer Treat Rev* 2008; **34:** 49–60.
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Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Mylotarg; ***USA:*** Mylotarg; ***Venez.:*** Mylotarg.