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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7. Robertson JF, *et al.* Endocrine treatment options for advanced breast cancer—the role of fulvestrant. *Eur J Cancer* 2005; **41:** 346–56.
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Preparations

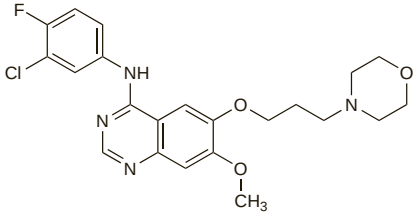
Proprietary Preparations (details are given in Part 3)
Arg.: Faslodex; ***Austral.:*** Faslodex; ***Belg.:*** Faslodex; ***Braz.:*** Faslodex; ***Canad.:*** Faslodex; ***Cz.:*** Faslodex; ***Denm.:*** Faslodex; ***Fin.:*** Faslodex; ***Fr.:*** Faslodex; ***Ger.:*** Faslodex; ***Gr.:*** Faslodex; ***Hung.:*** 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.

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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]

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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.

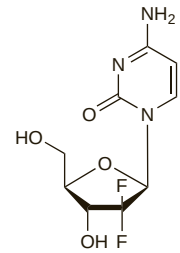
Gemcitabine Hydrochloride

(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