Flutamide *(BAN, USAN, rINN)*

Flutamid; Flutamida; Flutamidas; Flutamidi; Flutamidum; Sch-13521. α′,α′,α′-Trifluoro-4′-nitroisobutyro-*m*-toluidide; α,α,α-Trifluoro-2-methyl-4′-nitro-*m*-propionotoluidide.

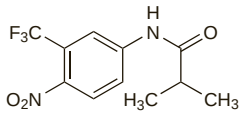
Флутамид

$C_{11}H_{11}F_3N_2O_3$ = 276.2.

CAS — 13311-84-7.

ATC — L02BB01.

ATC Vet — QL02BB01.



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

Ph. Eur. 6.2 (Flutamide). A pale yellow, crystalline powder. Practically insoluble in water; freely soluble in alcohol and in acetone. Protect from light.

USP 31 (Flutamide). A pale yellow, crystalline powder. Practically insoluble in water, in liquid paraffin, and in petroleum spirit; freely soluble in acetone, in ethyl acetate, and in methyl alcohol; soluble in chloroform and in ether. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

The most frequently reported adverse effects with flutamide are hot flushes and reversible gynaecomastia or breast tenderness, sometimes accompanied by galactorrhoea. Nausea, vomiting, diarrhoea, increased appetite, anorexia, and sleep disturbances may occur. There have been reports of skin reactions, including epidermal necrolysis, and of liver damage, sometimes fatal. Other adverse effects reported in patients receiving flutamide include anaemias, haemolysis, headache, dizziness, malaise, blurred vision, anxiety, depression, decreased libido, impotence, and hypertension. Abdominal pain, chest pain, dyspnoea, and cough have been reported rarely. Discoloration of the urine to amber or yellow-green can be caused by the presence of flutamide and/or its metabolites.

Flutamide should be used with care in patients with cardiovascular disease because of the possibility of fluid retention. It should also be used with caution in patients with hepatic impairment and is contra-indicated in those with severe impairment. Regular liver function testing is recommended in all patients: therapy should be stopped or dosage reduced if there is evidence of hepatotoxicity.

Effects on the blood. A report[1] of methaemoglobinaemia in an elderly man was attributed to flutamide. A study[2] of 45 patients given flutamide found no cases of methaemoglobinaemia, but the authors noted a further 3 published case reports.

1. Schott AM, *et al.* Flutamide-induced methemoglobinemia. *DICP Ann Pharmacother* 1991; **25:** 600–1.
2. Schulz M, *et al.* Lack of methemoglobinemia with flutamide. *Ann Pharmacother* 2001; **35:** 21–5.

Effects on the liver. Hepatitis occurred in a 79-year-old man taking flutamide 750 mg daily as sole therapy after a prostatectomy,[1] but a subsequent study[2] in 1091 patients given flutamide 250 mg three times daily as part of a regimen for prostate cancer found marked signs of liver damage only in 4, of whom only 2 had clinical evidence of hepatotoxicity. In the USA, the FDA had 46 reports of patients with hepatotoxicity associated with flutamide up to December 1994. Of these patients, 20 died from progressive liver disease.[3] Further cases have continued to be reported.[4-6] Early tapering of the dose, stopping therapy, or switching to another anti-androgen may resolve hepatotoxic effects.[7] Patients with chronic viral hepatitis may be at higher risk of developing hepatotoxicity with anti-androgen therapy.[8]

1. Hart W, Stricker BHC. Flutamide and hepatitis. *Ann Intern Med* 1989; **110:** 943–4.
2. Gomez J-L, *et al.* Incidence of liver toxicity associated with the use of flutamide in prostate cancer patients. *Am J Med* 1992; **92:** 465–70.
3. Wysowski DK, Fourcroy JL. Flutamide hepatotoxicity. *J Urol (Baltimore)* 1996; **155:** 209–12. Correction *ibid:* 396.
4. Garcia Cortes M, *et al.* Flutamide-induced hepatotoxicity: report of a case series. *Rev Esp Enferm Dig* 2001; **93:** 423–32. Correction. *ibid.*; 634.
5. Lubbert C, *et al.* Ikterus und schwere Leberfunktionsstorung bei der hormonablativen Behandlung des Prostatakarzinoms. *Internist (Berl)* 2004; **45:** 333–40.
6. Osculati A, Castiglioni C. Fatal liver complications with flutamide. *Lancet* 2006; **367:** 1140–1.
7. Lin ADY, *et al.* Antiandrogen-associated hepatotoxicity in the management of advanced prostate cancer. *J Chin Med Assoc* 2003; **66:** 735–40.
8. Pu Y-S, *et al.* Antiandrogen hepatotoxicity in patients with chronic viral hepatitis. *Eur Urol* 1999; **36:** 293–7.

Effects on the lungs. In a review[1] of 78 cases of pneumonitis reported to the FDA between 1998 and 2000 that were associated with bicalutamide, flutamide, or nilutamide, it was found that 14 patients had died of respiratory failure. It was estimated that the incidence of pneumonitis was highest for nilutamide (0.77%), but lower for flutamide (0.04%) and bicalutamide (0.01%).

1. Bennett CL, *et al.* Pneumonitis associated with nonsteroidal antiandrogens: presumptive evidence of a class effect. *Ann Intern Med* 2002; **137:** 625.

Effects on the skin. Photosensitivity reactions have been reported in patients receiving flutamide.[1,2] Some consider it to be an early manifestation of SLE.[2]

1. Fujimoto M, *et al.* Photosensitive dermatitis induced by flutamide. *Br J Dermatol* 1996; **135:** 496–7.
2. Kaur C, Thami GP. Flutamide-induced photosensitivity: is it a forme fruste of lupus? *Br J Dermatol* 2003; **148:** 603–4.

Gynaecomastia. Gynaecomastia (p.2092) and breast pain are frequent adverse effects of nonsteroidal anti-androgens used to treat prostate cancer. Nearly 90% of patients treated with bicalutamide in the Early Prostate Cancer programme experienced breast pain, gynaecomastia, or both.[1] Some patients who develop gynaecomastia will accept it as a tolerable adverse effect of therapy but others will require specific treatment, and a number of different measures have been tried for both prevention and treatment. The risk of breast changes can be reduced by the use of prophylactic low-dose irradiation of the breast area before nonsteroidal anti-androgen therapy is started. However, skin irritation can occur, and the long-term risk for development of breast cancer is unknown. Irradiation is unlikely to be effective once breast enlargement has occurred but it can help to reduce pain. Empirical use of oral analgesics or topical local anaesthetics may be considered for breast pain. Specific surgical treatment to reduce breast tissue includes liposuction and breast tissue excision.[2,3]

Hormonal therapy using tamoxifen or anastrozole has been suggested, largely based on reports of benefit in various patient groups with gynaecomastia.[1,2] Two randomised controlled studies[4,5] of men who were treated with bicalutamide for prostate cancer found that prophylactic tamoxifen was effective for the prevention of gynaecomastia and breast pain, but that anastrozole was no better than placebo. One of these studies[5] also assessed the use of these drugs as treatment and found that gynaecomastia and breast pain resolved in at least 65% of patients treated with tamoxifen, but only in about 18% of those treated with anastrozole. Tamoxifen is considered to be more effective than radiotherapy for prevention of gynaecomastia.[3]

1. Sieber PR. Treatment of bicalutamide-induced breast events. *Expert Rev Anticancer Ther* 2007; **7:** 1773–9.
2. Leibovitch I, *et al.* Management options for gynaecomastia and breast pain associated with nonsteroidal antiandrogen therapy: case studies in context. *Clin Drug Invest* 2003; **23:** 205–15.
3. Di Lorenzo G, *et al.* Management of gynaecomastia in patients with prostate cancer: a systematic review. *Lancet Oncol* 2005; **6:** 972–9.
4. Boccardo F, *et al.* Evaluation of tamoxifen and anastrozole in the prevention of gynecomastia and breast pain induced by bicalutamide monotherapy of prostate cancer. *J Clin Oncol* 2005; **23:** 808–15.
5. Saltzstein D, *et al.* Prevention and management of bicalutamide-induced gynecomastia and breast pain: randomized endocrinologic and clinical studies with tamoxifen and anastrozole. *Prostate Cancer Prostatic Dis* 2005; **8:** 75–83.

Interactions

Flutamide may increase the effect of warfarin, see Antineoplastics, p.1429.

Pharmacokinetics

Flutamide is reported to be rapidly and completely absorbed from the gastrointestinal tract with peak plasma concentrations occurring 1 hour after a dose. It is rapidly and extensively metabolised; the major metabolite (2-hydroxyflutamide) possesses anti-androgenic properties. The half-life of the metabolite is about 6 hours. Both flutamide and 2-hydroxyflutamide are more than 90% bound to plasma proteins. Excretion is mainly in the urine with only minor amounts appearing in the faeces.

◊ References.

1. Radwanski E, *et al.* Single and multiple dose pharmacokinetic evaluation of flutamide in normal geriatric volunteers. *J Clin Pharmacol* 1989; **29:** 554–8.

Uses and Administration

Flutamide is a nonsteroidal compound with anti-androgenic properties which appears to act by inhibiting the uptake and/or binding of androgens in target tissues. It is used, usually with gonadorelin analogues, in the palliative treatment of prostatic carcinoma (p.671). The usual oral dose is 250 mg three times daily. When used in combination therapy UK licensed product information recommends that flutamide treatment should be started at least 3 days before the gonadorelin analogue to suppress any 'flare' reaction; however, in some other countries it is recommended that treatment with both agents be begun simultaneously for optimum effect.

Congenital adrenal hyperplasia. For mention of the use of flutamide with testolactone to block androgenic effects in congenital adrenal hyperplasia, see p.1502.

Hirsutism. Anti-androgens (usually cyproterone or spironolactone) are widely used for the drug treatment of hirsutism (p.2089). Flutamide has no particular advantage in this context;[1,2] one study has found flutamide to be more effective than spironolactone in inhibiting hirsutism,[3] but others found them to be of similar efficacy,[4,5] and the risk of hepatotoxicity with flutamide is a problem.[2] Nonetheless, flutamide has continued to be investigated.[6-8]

1. Rittmaster RS. Hyperandrogenism—what is normal? *N Engl J Med* 1992; **327:** 194–6.
2. Rittmaster RS. Hirsutism. *Lancet* 1997; **349:** 191–5.
3. Cusan L, *et al.* Comparison of flutamide and spironolactone in the treatment of hirsutism: a randomized controlled trial. *Fertil Steril* 1994; **61:** 281–7.
4. Erenus M, *et al.* Comparison of the efficacy of spironolactone versus flutamide in the treatment of hirsutism. *Fertil Steril* 1994; **61:** 613–6.
5. Moghetti P, *et al.* Comparison of spironolactone, flutamide, and finasteride efficacy in the treatment of hirsutism: a randomized, double blind, placebo-controlled trial. *J Clin Endocrinol Metab* 2000; **85:** 89–94.
6. Muderris II, *et al.* Treatment of hirsutism with lowest-dose flutamide (62.5 mg/day). *Gynecol Endocrinol* 2000; **14:** 38–41.
7. Venturoli S, *et al.* Low-dose flutamide (125 mg/day) as maintenance therapy in the treatment of hirsutism. *Horm Res* 2001; **56:** 25–31.
8. Gambineri A, *et al.* Effect of flutamide and metformin administered alone or in combination in dieting obese women with polycystic ovary syndrome. *Clin Endocrinol (Oxf)* 2004; **60:** 241–9.

Malignant neoplasms. Androgen blockade, which may include the use of flutamide, is used in the management of metastatic hormone-responsive prostate cancer (p.671); once the cancer begins to progress despite such therapy, stopping flutamide occasionally produces paradoxical disease regression. Promising preliminary results have also followed the use of flutamide in patients with adenocarcinoma of the pancreas (p.671).

Polycystic ovary syndrome. Flutamide has been used, usually with metformin, in the management of polycystic ovary syndrome (p.2080);[1-4] additive effects have been reported with this combination.

1. Ibáñez L, *et al.* Additive effects of insulin-sensitizing and antiandrogen treatment in young nonobese women with hyperinsulinism, hyperandrogenism, dyslipidemia, and anovulation. *J Clin Endocrinol Metab* 2002; **87:** 2870–4.
2. Ibáñez L, *et al.* Low-dose flutamide-metformin therapy reverses insulin resistance and reduces fat mass in nonobese adolescents with ovarian hyperandrogenism. *J Clin Endocrinol Metab* 2003; **88:** 2600–6.
3. Gambineri A, *et al.* Effect of flutamide and metformin administered alone or in combination in dieting obese women with polycystic ovary syndrome. *Clin Endocrinol (Oxf)* 2004; **60:** 241–9.
4. Gambineri A, *et al.* Treatment with flutamide, metformin, and their combination added to a hypocaloric diet in overweight-obese women with polycystic ovary syndrome: a randomized, 12-month, placebo-controlled study. *J Clin Endocrinol Metab* 2006; **91:** 3970–80.

Preparations

USP 31: Flutamide Capsules.

Proprietary Preparations (details are given in Part 3)

Arg.: Asoflut; Dedile; Eulexin†; Flutaplex; Flutax†; Flutepan; Flutrax; FTDA†; Olter†; ***Austral.:*** Eulexin; Flutamin; Fugerel†; ***Austria:*** Afluta; Androbloc; Flutabene; Flutahexal; Flutastad; Fugerel; ***Belg.:*** Eulexin; Flutaplex; ***Braz.:*** Biomida†; Eulexin; Tecnoflut; Teflut; ***Canad.:*** Euflex; ***Chile:*** Androdor†; Drogenil; Etaconil; Flulem; ***Cz.:*** Andraxan; Flucinom; Flumed; Flutacan†; Flutaplex; Prostandril; Xadaren†; ***Denm.:*** Eulexin; Fluprosin; Flutacan†; Profamid; ***Fin.:*** Eulexin; Profamid; ***Fr.:*** Eulexine; Prostadirex; ***Ger.:*** Apimid†; Flumid; Fluta; Flutexin†; Fugerel; Prostica; Prostogenat†; Testotard†; ***Gr.:*** Adiprost; Andraxan; Elbat; Flucinom; Flutaplex; Palistop; Prostamide; Rikital; Tremexal; ***Hong Kong:*** Flutan†; Fugerel; ***Hung.:*** Cytamid†; Fluprost; Flutam; Flutasin; Fugerel; ***India:*** Cytomid; Prostamid; ***Indon.:*** Flutaplex; Fugerel; ***Irl.:*** Androstat; Drogenil; ***Israel:*** Eulexin; ***Ital.:*** Drogenil†; Eulexin; Fluprost; Virflutam†; ***Malaysia:*** Flutan†; Flutaplex; Fugerel†; ***Mex.:*** Eulexin; Flimutal; Fluken†; Flulem; Tafenil; ***Neth.:*** Drogenil; Eulexin; Flutaplex; Prostatil; ***Norw.:*** Eulexin; ***NZ:*** Eulexin; Flutamin; Flutol†; ***Philipp.:*** Fugerel; Prostanon; ***Pol.:*** Apo-Flutam; Fugerel; Prostandril; ***Port.:*** Drogenil; Eulexin; Prosneo; ***Rus.:*** Flutamid (Флутамид); Flutaplex (Флутаплекс); ***S.Afr.:*** Eulexin; Flutahexal; Flutaplex; ***Singapore:*** Flutan; Fugerel†; ***Spain:*** Eulexin; Flutandrona; Flutaplex†; Grisetin; Oncosal; Prostacur; ***Swed.:*** Eulexin; Flutacan†; ***Switz.:*** Flucinome; ***Thai.:*** Andraxan; Flulem; Flutan; Flutaplex; Fugerel; ***Turk.:*** Andraxan; Eulexin; ***UK:*** Chimax; Drogenil; ***USA:*** Eulexin†; ***Venez.:*** Etaconil; Eulexin.

Formestane *(BAN, rINN)* ⊗

CGP-32349; Formestaani; Formestan; Formestano; Formestanum; 4-Hydroxyandrostenedione; 4-OHA; 4-OHAD. 4-Hydroxyandrost-4-ene-3,17-dione.

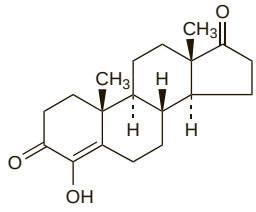
Форместан

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

CAS — 566-48-3.

ATC — L02BG02.

ATC Vet — QL02BG02.



Adverse Effects, Treatment, and Precautions

The most frequent adverse effects of formestane are local irritation and pain at the site of injection. Patients may experience hot flushes due to oestrogen deprivation. Other occasional or rare adverse effects include rashes and pruritus, alopecia or hypertrichosis, drowsiness, dizziness, emotional lability, oedema of the leg, thrombophlebitis, vaginal spotting or bleeding, gastrointestinal disturbances, pelvic or muscle cramps, arthralgia, exacerbation of bone pain, and a vasovagal reaction. Hypersensitivity reactions to the drug or the formulation have occurred.

Care should be taken to avoid intravascular injection. Injection into or near the sciatic nerve may result in pain and nerve trauma. Caution is required if patients drive or operate machinery.

Effects on carbohydrate metabolism. Recurrent hypoglycaemic episodes developed in a diabetic patient previously well maintained on gliclazide after addition of formestane to treatment for metastatic breast cancer.[1] Episodic hypoglycaemia continued after dosage reduction, and eventually withdrawal, of gliclazide, suggesting that the effect was not simply an interaction with the sulfonylurea.

1. Brankin E, *et al.* Hypoglycaemia associated with formestane treatment. *BMJ* 1997; **314:** 869.

Pharmacokinetics

Intramuscular formestane is reported to form a depot that slowly releases active drug into the systemic circulation; maximum plasma concentrations occur about 30 to 48 hours after a single dose and then decline fairly rapidly over 2 to 4 days before declining more slowly, with an apparent elimination half-life of 5 to 6 days. The systemic uptake has been estimated at 20 to 25% of the dose in 14 days. Formestane is about 85% bound to plasma protein in the circulation. It is metabolised by conjugation to the inactive glucuronide: less than 1% of the dose is excreted in urine unchanged.

Uses and Administration

Formestane is an inhibitor of the aromatase (oestrogen synthetase) system which is responsible for the production of oestrogens from androgens. It has been used for its anti-oestrogenic properties in the endocrine treatment of advanced breast cancer in postmenopausal women (p.661).

It is given by intramuscular injection, as an aqueous suspension, in doses of 250 mg every 2 weeks. Injections should be given into each buttock alternately.

◊ Reviews.

1. Wiseman LR, McTavish D. Formestane: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in the management of breast cancer and prostatic cancer. *Drugs* 1993; **45:** 66–84.
2. Anonymous. Formestane for advanced breast cancer in postmenopausal women. *Drug Ther Bull* 1993; **31:** 85–7.
3. Carlini P, *et al.* Formestane, a steroidal aromatase inhibitor after failure of non-steroidal aromatase inhibitors (anastrozole and letrozole): is a clinical benefit still achievable? *Ann Oncol* 2001; **12:** 1539–43.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Lentaron†; ***Austria:*** Lentaron; ***Braz.:*** Lentaron†; ***Chile:*** Lentaron†; ***Cz.:*** Lentaron†; ***Denm.:*** Lentaron†; ***Ger.:*** Lentaron†; ***Gr.:*** Lentaron†; ***Hong Kong:*** Lentaron†; ***Ital.:*** Lentaron†; ***Malaysia:*** Lentaron†; ***S.Afr.:*** Lentare†; ***Spain:*** Lentaron†; ***Turk.:*** Lentaron.

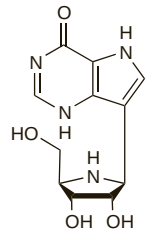
Forodesine Hydrochloride *(USAN, rINNM)*

BCX-1777 (forodesine or forodesine hydrochloride); Forodésine, Chlorhydrate de; Forodesini Hydrochloridum; Hidrocloruro de forodesina. (–)-7-[(2*S*,3*S*,4*R*,5*R*)-3,4-Dihydroxy-5-(hydroxymethyl)pyrrolidin-2-yl]-1,5-dihydro-4*H*-pyrrolo[3,2-*d*]pyrimidin-4-one hydrochloride.

Фородезина Гидрохлорид

$C_{11}H_{14}N_4O_4$,HCl = 302.7.

CAS — 209799-67-7 (forodesine); 284490-13-7 (forodesine hydrochloride).



(forodesine)

Profile

Forodesine is an inhibitor of purine nucleoside phosphorylase. It is under investigation in the treatment of T-cell lymphomas, chronic lymphocytic leukaemia, and acute lymphoblastic leukaemia.

Fotemustine *(BAN, rINN)*

Fotemustin; Fotemustina; Fotémustine; Fotemustinum; S-10036. (±)-Diethyl {1-[3-(2-chloroethyl)-3-nitrosoureido]ethyl}phosphonate.

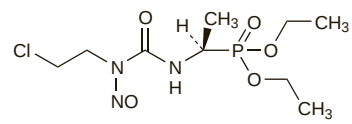
Фотемустин

$C_9H_{19}ClN_3O_5P$ = 315.7.

CAS — 92118-27-9.

ATC — L01AD05.

ATC Vet — QL01AD05.



Profile

Fotemustine is a nitrosourea derivative and alkylating agent with actions similar to those of carmustine (p.694). It is used in the treatment of disseminated malignant melanoma, particularly where cerebral metastases are present (p.673) and has been tried in primary malignancies of the brain (p.660). When used as a single agent it is licensed for intravenous or intra-arterial infusion in usual doses of 100 mg/m^2 weekly for 3 weeks to induce remission, followed after 4 to 5 weeks, if blood counts permit, by maintenance dosage with 100 mg/m^2 every 3 weeks. Intravenous infusions are given over 1 hour and intra-arterial infusions over 4 hours. Liver function should be monitored regularly during induction treatment. Regular blood counts should be taken and dosage should be reduced or withheld if white cell or platelet counts are below acceptable levels (see also Bone-marrow Depression, p.639). Bone-marrow suppression may be delayed, with the nadir of the white cell counts 5 or 6 weeks after dosing. Solutions for infusion must be freshly prepared and protected from light.

◊ References.

1. Rougier P, *et al.* Fotemustine in patients with advanced gastric cancer, a phase II trial from the EORTC-GITCCG. *Eur J Cancer* 1996; **32A:** 1432–3.
2. Marzolini C, *et al.* Pharmacokinetics of temozolomide in association with fotemustine in malignant melanoma and malignant glioma patients: comparison of oral, intravenous, and hepatic intra-arterial administration. *Cancer Chemother Pharmacol* 1998; **42:** 433–40.
3. Ulrich J, *et al.* Management of cerebral metastases from malignant melanoma: results of a combined, simultaneous treatment with fotemustine and irradiation. *J Neurooncol* 1999; **43:** 173–8.
4. Terheyden P, *et al.* Sequential interferon-alpha2b, interleukin-2 and fotemustine for patients with metastatic melanoma. *Melanoma Res* 2000; **10:** 475–82.
5. Frenay M, *et al.* Up-front chemotherapy with fotemustine (F) / cisplatin (CDDP) / etoposide (VP16) regimen in the treatment of 33 non-removable glioblastomas. *Eur J Cancer* 2000; **36:** 1026–31.
6. Mornex F, *et al.* A prospective randomized multicentre phase III trial of fotemustine plus whole brain irradiation versus fotemustine alone in cerebral metastases of malignant melanoma. *Melanoma Res* 2003; **13:** 97–103.
7. Aapro MS, *et al.* Phase II study of fotemustine in patients with advanced ovarian carcinoma: a trial of the EORTC Gynecological Cancer Group. *Eur J Cancer* 2003; **39:** 1141–13.
8. Fazeny-Dorner B, *et al.* Second-line chemotherapy with dacarbazine and fotemustine in nitrosourea-pretreated patients with recurrent glioblastoma multiforme. *Anticancer Drugs* 2003; **14:** 437–42.
9. Avril MF, *et al.* Fotemustine compared with dacarbazine in patients with disseminated malignant melanoma: a phase III study. *J Clin Oncol* 2004; **22:** 1118–25.
10. Ozkan M, *et al.* Post-operative sequential chemo-radiotherapy in high-grade cerebral gliomas with fotemustine. *J Chemother* 2004; **16:** 298–302.
11. Bonenkamp JJ, *et al.* Isolated limb infusion with fotemustine after dacarbazine chemosensitisation for inoperable loco-regional melanoma recurrence. *Eur J Surg Oncol* 2004; **30:** 1107–12.
12. Peters S, *et al.* Intra-arterial hepatic fotemustine for the treatment of liver metastases from uveal melanoma: experience in 101 patients. *Ann Oncol* 2006; **17:** 578–83.
13. Gill S, *et al.* Long-term survival and secondary acute leukemia after fotemustine therapy for metastatic melanoma. *J Clin Oncol* 2007; **25:** 4493–4.
14. Scoccianti S, *et al.* Second-line chemotherapy with fotemustine in temozolomide-pretreated patients with relapsing glioblastoma: a single institution experience. *Anticancer Drugs* 2008; **19:** 613–20.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Muforan†; ***Austral.:*** Muphoran; ***Austria:*** Muphoran; ***Belg.:*** Muphoran; ***Braz.:*** Muphoran; ***Cz.:*** Mustophoran; ***Fr.:*** Muphoran; ***Gr.:*** Muphoran; ***Hung.:*** Mustophoran; ***Israel:*** Muphoran; ***Ital.:*** Muphoran; ***NZ:*** Muphoran; ***Pol.:*** Mustophoran; ***Port.:*** Muphoran; ***Rus.:*** Mustophoran (Мюстофоран); ***Spain:*** Mustoforan; ***Turk.:*** Muphoran.

Fulvestrant *(BAN, USAN, rINN)* ⊗

Fulvestrantum; ICI-182780; ZD-9238. 7α-[9-(4,4,5,5,5-Pentafluoropentylsulfinyl)nonyl]estra-1,3,5(10)-triene-3,17β-diol.

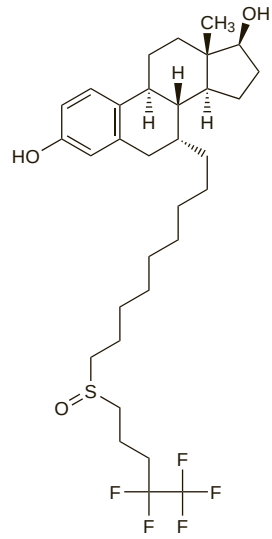
Фульвестрант

$C_{32}H_{47}F_5O_3S$ = 606.8.

CAS — 129453-61-8.

ATC — L02BA03.

ATC Vet — QL02BA03.



Pharmacopoeias. In *US.*

USP 31 (Fulvestrant). A mixture of the diastereoisomers A and B. A white powder. Freely soluble in alcohol. Store at a temperature of 2° to 8°. Protect from light.

Adverse Effects and Precautions

The most commonly reported adverse effects of fulvestrant are nausea, vomiting, constipation, diarrhoea, abdominal pain, headache, back pain, hot flushes, and pharyngitis. Injection site reactions can occur. Other adverse effects include rash, asthenia, urinary-tract infections, venous thromboembolism, and elevations in liver enzyme values. Myalgia, vertigo, and leucopenia have been reported. Hypersensitivity reactions, including angioedema and urticaria, can occur. Vaginal bleeding has been reported rarely. Fulvestrant should be given with caution to those with severe renal impairment (creatinine clearance less than 30 mL/minute) and in those with mild to moderate hepatic impairment; use is contra-indicated in those with severe hepatic impairment. In patients with bleeding tendencies, thrombocytopenia, or taking anticoagulants, fulvestrant should also be used with caution, if at all.

Pharmacokinetics

Fulvestrant is slowly absorbed after intramuscular injection; maximum plasma concentrations are reached after about 7 days. Steady-state concentrations are reached after about 3 to 6 doses (given monthly). Fulvestrant is highly bound to plasma proteins. It is metabolised primarily in the liver to a number of metabolites,