and, given the pharmacokinetic variability seen with etoposide, the authors considered any clinical impact to be small.

1. Relling MV, *et al.* Etoposide pharmacokinetics and pharmacodynamics after acute and chronic exposure to cisplatin. *Clin Pharmacol Ther* 1994; **56:** 503–11.
2. Thomas HD, *et al.* Randomized cross-over clinical trial to study potential pharmacokinetic interactions between cisplatin or carboplatin and etoposide. *Br J Clin Pharmacol* 2002; **53:** 83–91.

Ciclosporin. High-dose ciclosporin therapy was found to increase the exposure to etoposide by 80%, and to reduce etoposide clearance by 38%. Leucopenia was increased. Etoposide doses should be halved when the drug is given with high-dose ciclosporin.[1] In a study[2] of children who received etoposide and mitoxantrone for acute myeloid leukaemia, the addition of ciclosporin with a 40% reduction in the doses of the antineoplastics still resulted in a 71% reduction in the clearance of etoposide, and a 42% reduction for mitoxantrone. However, there was wide interpatient variability, and the rates of stomatitis and infection were similar between the groups, with or without ciclosporin.

1. Lum BL, *et al.* Alteration of etoposide pharmacokinetics and pharmacodynamics by cyclosporine in a phase I trial to modulate drug resistance. *J Clin Oncol* 1992; **10:** 1635–42.
2. Lacayo NJ, *et al.* Pharmacokinetic interactions of cyclosporine with etoposide and mitoxantrone in children with acute myeloid leukemia. *Leukemia* 2002; **16:** 920–7.

Grapefruit juice. In a randomised crossover study[1] of 6 patients, grapefruit juice appeared to reduce the oral bioavailability of etoposide. Initially the authors had expected the opposite since etoposide is demethylated by cytochrome P450 isoenzyme CYP3A4. Although no definite conclusions could be made due to the small number of patients studied, a possible mechanism might have been alteration of P-glycoprotein mediated transport.

1. Reif S, *et al.* Effect of grapefruit juice intake on etoposide bioavailability. *Eur J Clin Pharmacol* 2002; **58:** 491–4.

Pharmacokinetics

Absorption after oral doses is variable, but on average about 50% of the dose of etoposide is absorbed. The pharmacokinetics of etoposide are subject to considerable interindividual variation. It is rapidly distributed, and concentrations in plasma fall in a biphasic manner, with a terminal half-life of 4 to 11 hours. Etoposide is about 94% bound to plasma protein. It is metabolised by the cytochrome P450 isoenzyme CYP3A4. Etoposide is excreted in urine and faeces as unchanged drug and metabolites: about 45% of a dose is reported to be excreted in urine over 72 hours. It crosses the blood-brain barrier poorly; concentrations in CSF are 1 to 10% of those in plasma. It is distributed into breast milk (see Breast Feeding, above).

◊ References.

1. Toffoli G, *et al.* Pharmacokinetic optimisation of treatment with oral etoposide. *Clin Pharmacokinet* 2004; **43:** 441–66.

Metabolism. Studies *in vitro* suggested that metabolic activation of etoposide by oxidation into the *O*-quinone derivative might play an essential role in its activity against DNA.[1]

1. van Maanen JMS, *et al.* Metabolic activation of anti-tumour agent VP 16-213. *Hum Toxicol* 1986; **5:** 136.

Uses and Administration

Etoposide is a semisynthetic derivative of podophyllotoxin with antineoplastic properties; it interferes with the function of topoisomerase II thus inhibiting DNA synthesis, and is most active against cells in the late S and G_2 phases of the cell cycle.

It is used, usually with other antineoplastics, in the treatment of tumours of the testis, small cell cancer of the lung, and in acute leukaemias. It has also been tried in other solid tumours including those of the brain, gastrointestinal tract, ovary, and thymus, and some childhood neoplasms; in lymphomas, and in the treatment of Kaposi's sarcoma associated with AIDS. For further discussion, see the cross-references indicated under Malignant Neoplasms, below.

Etoposide is given by slow intravenous infusion over at least 30 minutes, as a solution in sodium chloride 0.9% or glucose 5% injection. In general, the concentration of the infusion should be between 200 to 400 micrograms/mL, although recommendations vary depending on the preparation; precipitation may occur at higher concentrations. Etoposide phosphate, a prodrug, has improved solubility in water. 113.6 mg of etoposide phosphate is equivalent to 100 mg of etoposide. Intravenous doses are calculated in terms of etoposide, and are identical to those of the base, but it may be given in concentrations up to the equivalent of etoposide 20 mg/mL. Etoposide phosphate solutions may be infused over 5 minutes to 3.5 hours. Etoposide may also be given orally.

Regimens vary; the usual intravenous dose of etoposide ranges from 50 to 120 mg/m^2 daily for 5 days. Somewhat lower doses have been suggested in lung cancer. Alternatively, 100 mg/m^2 has been given on alternate days to a total of 300 mg/m^2. The usual oral dose of etoposide is 100 to 240 mg/m^2 daily for 5 consecutive days. Courses may be repeated after 3 to 4 weeks. Doses should be reduced in renal impairment (see below).

Administration. Although precipitation of etoposide may occur at high infusion concentrations (see Uses and Administration, above), high doses of etoposide have been infused undiluted to avoid giving large volumes of fluid to the patient.[1-3] Etoposide was infused through a central line, and this method has been reported to be safe and effective;[2] pharmacokinetic studies suggested unaltered systemic bioavailability when compared with diluted infusions.[3] However, cracking of plastic syringes and infusion cassettes has been reported, possibly due to the polyethylene glycol component of the formulation. This appears particularly problematic when devices containing ABS plastic (a polymer produced from acrylonitrile, butadiene, and styrene) are used; alternative devices may be preferable.[1]

Etoposide has been injected into the ventricles of the brain in the treatment of patients with neoplastic meningitis.[4]

1. Schwinghammer TL, *et al.* Cracking of ABS plastic devices used to infuse undiluted etoposide injection. *Am J Hosp Pharm* 1988; **45:** 1277.
2. Creger RJ, *et al.* Infusion of high doses of undiluted etoposide through central venous catheters during preparation for bone marrow transplantation. *Cancer Invest* 1990; **8:** 13–16.
3. Ehninger G, *et al.* Unaltered pharmacokinetics after the administration of high-dose etoposide without prior dilution. *Cancer Chemother Pharmacol* 1991; **28:** 214–16.
4. Chamberlain MC, *et al.* Phase II trial of intracerebrospinal fluid etoposide in the treatment of neoplastic meningitis. *Cancer* 2006; **106:** 2021–7.

Administration in renal impairment. Some licensed product information for etoposide or etoposide phosphate recommends that patients with a creatinine clearance of between 15 and 50 mL/minute be given 75% of the recommended dose. No recommendations are given for those patients having a creatinine clearance of below 15 mL/minute, although one product (*Vepesid; BMS, USA*) suggests that further dose reduction in these patients be considered.

Blood disorders, non-malignant. For reference to the use of combination chemotherapy, including etoposide, in a few patients with refractory idiopathic thrombocytopenic purpura, see p.1505.

Histiocytic syndromes. Systemic chemotherapy is often tried in patients with extensive Langerhans-cell histiocytosis (p.650), although its value is uncertain. Etoposide is one of the drugs widely used for this purpose.

Hypereosinophilic syndrome. Etoposide has been reported to produce clinical responses in patients with the hypereosinophilic syndrome.[1]

1. Bourrat E, *et al.* Etoposide for treating the hypereosinophilic syndrome. *Ann Intern Med* 1994; **121:** 899–900.

Malignant neoplasms. Etoposide has been used for a variety of solid tumours: in particular it is part of curative regimens used in the treatment of testicular cancer and germ-cell tumours of the ovary (see p.673 and p.670), and is used with cisplatin and other drugs in the treatment of lung cancer (p.668). Other solid neoplasms in which it is sometimes employed include those of the brain (p.660), stomach (p.664), and thymus (p.674), as well as in neuroblastoma (p.674), Wilms' tumour (p.667), retinoblastoma (p.675), and rhabdomyosarcoma (p.676); it has also formed part of systemic regimens for bone sarcomas (p.675), disseminated Kaposi's sarcoma (see p.675), and gestational trophoblastic tumours (p.650). Etoposide is used in regimens for Hodgkin's disease (see p.655); it is also sometimes used in aggressive intermediate- and high-grade non-Hodgkin's lymphomas (p.656), and may produce short-term responses in mycosis fungoides (p.657). It is also used in Burkitt's lymphoma (p.657). Etoposide may have benefits when added to induction protocols for acute myeloid leukaemia (p.652), and when used as part of intensification therapy in acute lymphoblastic leukaemia (p.651). It has formed part of salvage regimens in multiple myeloma (p.658).

Vasculitic syndromes. For mention of the use of etoposide to induce remission in patients with Wegener's granulomatosis resistant to standard therapy with cyclophosphamide and corticosteroids, see p.1515.

Preparations

BP 2008: Etoposide Capsules; Etoposide Intravenous Infusion;
USP 31: Etoposide Capsules; Etoposide Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Citodox; Etocris; Etopofos†; Euvaxon; Labimion†; Neoplaxol; Optasid†; Percas; Vepesid; VP-Gen; ***Austral.:*** Etopophos; Vepesid; ***Austria:*** Etopofos; Vepesid; ***Belg.:*** Celltop; Eposin; Etopophos†; Vepesid; ***Braz.:*** Eposido; Etopos†; Etopul†; Etosin; Eunades; Evoposdo†; Nexvep; Posidon; Vepesid; ***Canad.:*** Vepesid; ***Chile:*** Epsidox; Lastet†; ***Cz.:*** Etopophos†; Lastet; Vepesid; ***Denm.:*** Etopofos; Vepesid; ***Fin.:*** Eposin†; Etopofos; Exitop†; Vepesid; ***Fr.:*** Celltop; Etopophos; Vepeside; ***Ger.:*** ETO CS; Eto-cell; Eto-Gry; Etomedac; Etopophos; Exitop; Neoposid; Onkoposid; Riboposid; Vepesid; ***Gr.:*** Etobion; Vepesid; ***Hong Kong:*** Vepesid; ***Hung.:*** Lastet; Sintopozid; Vepesid; ***India:*** Bioposide; Etosid; Lastet†; Posid; ***Indon.:*** Posyd; ***Irl.:*** Etopophos†; Vepesid; ***Israel:*** Etopophos†; Vepesid†; ***Ital.:*** Lastet; Vepesid; ***Jpn:*** Lastet; ***Malaysia:*** Eposin; Lastet; Vepesid†; ***Mex.:*** Etonco; Etopos; Kenazol; Lastet†; Vepesid; VP-Tec; ***Neth.:*** Toposin; Vepesid; ***Norw.:*** Eposin; Etopofos; Vepesid; ***NZ:*** Etopophos; Vepesid; ***Philipp.:*** Etopoxan; Etopul; Fytosid; Lastet; Posid; Topresid; Vepesid; ***Pol.:*** Lastet; Sintopozid; Vepesid; ***Port.:*** Eposin; Lastet; Vepesid; ***Rus.:*** Etopos (Этопос)†; Vepesid (Вепезид); ***S.Afr.:*** Eposin; Etopophos; Vepesid; ***Singapore:*** Lastet; Vepesid†; ***Spain:*** Eposin†; Lastet; Vepesid; ***Swed.:*** Eposin; Etopofos; Exitop†; Vepesid; ***Switz.:*** Etopophos; Vepesid; ***Thai.:*** Eposin; Etopos; Fytosid; Lastet; Vepesid; ***Turk.:*** Eposin; Lastet; Vepesid; ***UK:*** Eposin; Etopophos; Vepesid; ***USA:*** Etopophos; Toposar; Vepesid; ***Venez.:*** Etonolver; Etosid; Fytosid.

Exemestane *(BAN, USAN, rINN)* ⊗

Eksemestaani; Eksemestan; Exemestan; Exémestane; Exemestano; Exemestanum; FCE-24304. 6-Methyleneandrosta-1,4-diene-3,17-dione.

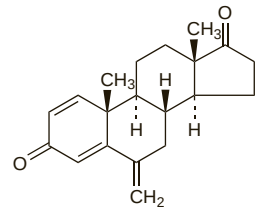
Эксеместан

$C_{20}H_{24}O_2$ = 296.4.

CAS — 107868-30-4.

ATC — L02BG06.

ATC Vet — QL02BG06.



Adverse Effects and Precautions

The most frequently reported adverse effects for exemestane are gastrointestinal disturbances, hot flushes, arthralgia, myalgia, sweating, fatigue, and dizziness. Other reported effects include headache, insomnia, somnolence, depression, skin rashes, alopecia, asthenia, and peripheral and leg oedema. Thrombocytopenia and leucopenia have been reported occasionally. Reductions in bone mineral density can occur with long-term use of exemestane. Density should therefore be assessed at the start of therapy, in those with osteoporosis or at risk of it, and patients monitored during therapy.

The use of exemestane is contra-indicated in premenopausal women (particularly in pregnancy).

Effects on the musculoskeletal system. Exemestane therapy has been found to decrease bone mineral density (BMD) in postmenopausal women with early breast cancer.[1,2] In one study, the decrease in BMD was seen within 6 months of switching therapy from tamoxifen, and was significant at the lumbar spine and hip.[2] In a Scandinavian study, BMD loss with exemestane compared with placebo was modest from the femoral neck, and not significant at the lumbar spine;[1] however, it was noted that the changes in the placebo group were greater than expected, possibly due to the lack of calcium and vitamin D supplementation, and that there is a high incidence of hip fracture in Scandinavia. Patients starting exemestane therapy should be assessed for baseline BMD;[1] while those with normal BMD are considered to not need further assessment beyond lifestyle advice, those with osteopenia should have their BMD monitored, and therapeutic interventions made as appropriate.[2]

1. Lønning PE, *et al.* Effects of exemestane administered for 2 years versus placebo on bone mineral density, bone biomarkers, and plasma lipids in patients with surgically resected early breast cancer. *J Clin Oncol* 2005; **23:** 5126–37.
2. Coleman RE, *et al.* Skeletal effects of exemestane on bone-mineral density, bone biomarkers, and fracture incidence in postmenopausal women with early breast cancer participating in the Intergroup Exemestane Study (IES): a randomised controlled study. *Lancet Oncol* 2007; **8:** 119–27.

Interactions

The metabolism of exemestane is mediated by the cytochrome P450 isoenzyme CYP3A4. Rifampicin, a potent inducer of CYP isoenzymes, can decrease plasma concentrations of exemestane. Use with other drugs that induce this isoenzyme may reduce the efficacy of exemestane. Exemestane should also be used cautiously with drugs that are substrates for CYP3A4

and that have a narrow therapeutic index. Significant effects on exemestane clearance by cytochrome P450 isoenzyme inhibitors are considered unlikely. Exemestane should not be given with oestrogen-containing drugs as these would negate its pharmacological action.

Pharmacokinetics

Exemestane is rapidly absorbed from the gastrointestinal tract. Its bioavailability is limited by first-pass metabolism, but is increased when taken with food. Exemestane is widely distributed, and is extensively bound to plasma proteins. It is metabolised via oxidation by the cytochrome P450 isoenzyme CYP3A4, and via reduction by aldoketoreductase. Metabolites are excreted in the urine and faeces, and less than 1% of a dose is excreted unchanged in the urine. Exemestane has a terminal elimination half-life of about 24 hours.

Uses and Administration

Exemestane is a selective inhibitor of the aromatase (oestrogen synthase) system, similar to formestane (p.726). It is used in the treatment of advanced breast cancer (p.661), in postmenopausal women who are no longer responsive to anti-oestrogen therapy. It is also used for adjuvant treatment of postmenopausal women with oestrogen-receptor positive early breast cancer, after 2 to 3 years of initial adjuvant tamoxifen treatment; a total of 5 years of adjuvant hormonal therapy should be given. The recommended oral dose is 25 mg once daily, preferably after a meal.

In patients receiving potent inducers of the cytochrome P450 isoenzyme CYP3A4 (such as rifampicin or phenytoin), the recommended oral dose of exemestane is 50 mg once daily, after a meal.

◊ References.

1. Clemett D, Lamb HM. Exemestane: a review of its use in postmenopausal women with advanced breast cancer. *Drugs* 2000; **59:** 1279–96.
2. Kaufmann M, *et al.* Exemestane is superior to megestrol acetate after tamoxifen failure in postmenopausal women with advanced breast cancer: results of a phase III randomized double-blind trial. *J Clin Oncol* 2000; **18:** 1399–1411.
3. Lønning PE, *et al.* Activity of exemestane in metastatic breast cancer after failure of nonsteroidal aromatase inhibitors: a phase II trial. *J Clin Oncol* 2000; **18:** 2234–44.
4. Coombes RC, *et al.* A randomized trial of exemestane after two to three years of tamoxifen therapy in postmenopausal women with primary breast cancer. *N Engl J Med* 2004; **350:** 1081–92. Corrections. *ibid.*; **351:** 2461 and *ibid.* 2006; **355:** 1746.
5. Bertelli G, *et al.* Sequential treatment with exemestane and nonsteroidal aromatase inhibitors in advanced breast cancer. *Oncology* 2006; **69:** 471–7.
6. Bundred N. The evolving role of exemestane in the management of breast cancer. *Br J Hosp Med* 2006; **67:** 427–30.
7. Coombes RC, *et al.* Survival and safety of exemestane versus tamoxifen after 2-3 years' tamoxifen treatment (Intergroup Exemestane Study): a randomised controlled trial. *Lancet* 2007; **369:** 559–70. Correction. *ibid.*; 906.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Aromasin; ***Austral.:*** Aromasin; ***Austria:*** Aromasin; ***Belg.:*** Aromasin; ***Braz.:*** Aromasin; ***Canad.:*** Aromasin; ***Chile:*** Aromasin; ***Cz.:*** Aromasin; ***Denm.:*** Aromasin; ***Fin.:*** Aromasin; ***Fr.:*** Aromasine; ***Ger.:*** Aromasin; ***Gr.:*** Aromasin; ***Hong Kong:*** Aromasin; ***Hung.:*** Aromasin; ***Indon.:*** Aromasin; ***Irl.:*** Aromasin; ***Israel:*** Aromasin; ***Ital.:*** Aromasin; ***Malaysia:*** Aromasin; ***Neth.:*** Aromasin; ***Norw.:*** Aromasin; ***NZ:*** Aromasin; ***Philipp.:*** Aromasin; ***Pol.:*** Aromasin; ***Port.:*** Aromasin; ***Rus.:*** Aromasin (Аромазин); ***S.Afr.:*** Aromasin; ***Singapore:*** Aromasin; ***Spain:*** Aromasil; ***Swed.:*** Aromasin; ***Switz.:*** Aromasin; ***Thai.:*** Aromasin; ***Turk.:*** Aromasin; ***UK:*** Aromasin; ***USA:*** Aromasin; ***Venez.:*** Aromasin.

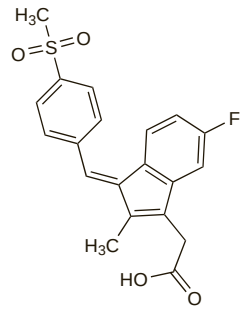
Exisulind *(rINN)*

Exisulindum; FGN-1; Sulindac Sulfone. 5-Fluoro-2-methyl-1-[(*Z*)-*p*-(methylsulfonyl)benzylidene]indene-3-acetic acid.

Эксисулинд

$C_{20}H_{17}FO_4S$ = 372.4.

CAS — 59973-80-7.



Profile

Exisulind is a sulfone metabolite of sulindac (p.126) that is reported to induce apoptosis in cancerous and precancerous cells. It has been studied for the treatment of familial adenomatous polyposis, with variable results. It is also being investigated for the prevention and treatment of malignant neoplasms, including those of the breast, prostate, and lung.

◊ References.

1. Goluboff ET. Exisulind, a selective apoptotic antineoplastic drug. *Expert Opin Invest Drugs* 2001; **10:** 1875–82.
2. Webster WS, Leibovich BC. Exisulind in the treatment of prostate cancer. *Expert Rev Anticancer Ther* 2005; **5:** 957–62.
3. Arber N, *et al.* Sporadic adenomatous polyp regression with exisulind is effective but toxic: a randomised, double blind, placebo controlled, dose-response study. *Gut* 2006; **55:** 367–73.

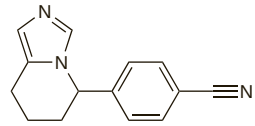
Fadrozole Hydrochloride *(USAN, rINNM)* ⊗

CGS-16949 (fadrozole); CGS-16949A; Fadrozole, Chlorhydrate de; Fadrozoli Hydrochloridum; Hidrocloruro de fadrozol. (±)-*p*-(5,6,7,8-Tetrahydroimidazo[1,5-*a*]pyridin-5-yl)benzonitrile monohydrochloride.

Фадрозола Гидрохлорид

$C_{14}H_{13}N_3HCl$ = 259.7.

CAS — 102676-47-1 (fadrozole); 102676-96-0 (fadrozole hydrochloride).



(fadrozole)

Profile

Fadrozole hydrochloride is a selective nonsteroidal inhibitor of the aromatase (oestrogen synthetase) system, similar to anastrozole (p.681). It is used for the treatment of breast cancer. It has been given in oral doses of 1 mg twice daily.

◊ References.

1. Buzdar AU, *et al.* Fadrozole HCl (CGS-16949A) versus megestrol acetate treatment of postmenopausal patients with metastatic breast carcinoma: results of two randomized double blind controlled multiinstitutional trials. *Cancer* 1996; **77:** 2503–13.
2. Miller AA, *et al.* Fadrozole hydrochloride in postmenopausal patients with metastatic breast carcinoma. *Cancer* 1996; **78:** 789–93.
3. Falkson CI, Falkson HC. A randomised study of CGS 16949A (fadrozole) versus tamoxifen in previously untreated postmenopausal patients with metastatic breast cancer. *Ann Oncol* 1996; **7:** 465–9.
4. Thurlimann B, *et al.* First-line fadrozole HCl (CGS 16949A) versus tamoxifen in postmenopausal women with advanced breast cancer: prospective randomised trial of the Swiss Group for Clinical Cancer Research SAKK 20/88. *Ann Oncol* 1996; **7:** 471–9.
5. Tominaga T, *et al.* Double-blind randomised trial comparing the non-steroidal aromatase inhibitors letrozole and fadrozole in postmenopausal women with advanced breast cancer. *Ann Oncol* 2003; **14:** 62–70.

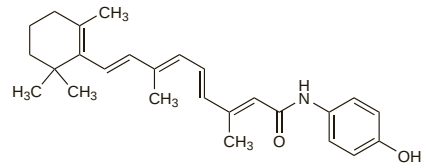
Fenretinide *(USAN, rINN)*

Fenretinida; Fenrétinide; Fenretinidum; 4-HPR; 4-Hydroxyphenylretinamide; McN-R-1967. *all-trans*-4′-Hydroxyretinanilide.

Фенретинид

$C_{26}H_{33}NO_2$ = 391.5.

CAS — 65646-68-6.



Profile

Fenretinide is a retinoid derivative that is given orally and is being studied in the management of breast and prostate cancer, malignant bone tumours, soft-tissue sarcoma, and some other malignancies. It has also been tried in oral lichen planus and leucoplakia. Fenretinide has been investigated in the treatment of psoriasis, but was associated with unacceptable adverse effects such as night blindness and severe toxic erythema.

◊ Fenretinide has been studied for the treatment of breast cancer and cutaneous malignancies but early results were disappointing and night blindness and mucocutaneous effects have been associated with this use.[1] Fenretinide has been investigated for the prevention of breast cancer (p.662), but a large randomised study of secondary prevention failed to show any benefit.[2] A follow-up of the same study[3] found that patients receiving fenretinide had a lower incidence of ovarian carcinoma during the 5-year treatment period, but that this apparently protective effect disappeared after treatment was stopped. Combinations of tamoxifen and fenretinide, given intermittently (for treatment or prevention), have been reported to be well tolerated.[4-6]

1. Modiano MR, *et al.* Phase II study of fenretinide (N-[4-hydroxyphenyl]retinamide) in advanced breast cancer and melanoma. *Invest New Drugs* 1990; **8:** 317–19.
2. Veronesi U, *et al.* Randomized trial of fenretinide to prevent second breast malignancy in women with early breast cancer. *J Natl Cancer Inst* 1999; **91:** 1847–56.
3. De Palo G, *et al.* Effect of fenretinide on ovarian carcinoma occurrence. *Gynecol Oncol* 2002; **86:** 24–7.
4. Cobleigh MA, *et al.* Phase I/II trial of tamoxifen with or without fenretinide, an analog of vitamin A, in women with metastatic breast cancer. *J Clin Oncol* 1993; **11:** 474–7.
5. Conley B, *et al.* Pilot trial of the safety, tolerability, and retinoid levels of N-(4-hydroxyphenyl) retinamide in combination with tamoxifen in patients at high risk for developing invasive breast cancer. *J Clin Oncol* 2000; **18:** 275–83.
6. Guerrieri-Gonzaga A. *et al.* Preliminary results on safety and activity of a randomized, double-blind, 2 x 2 trial of low-dose tamoxifen and fenretinide for breast cancer prevention in premenopausal women. *J Clin Oncol* 2006; **24:** 129–35.

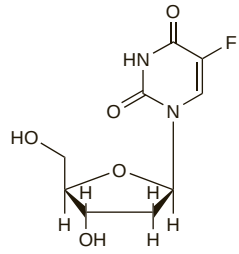
Floxuridine *(USAN, rINN)*

Floxuridina; Floxuridinum; 5-Fluorouracil Deoxyriboside; FUDR; NSC-27640; WR-138720. 2′-Deoxy-5-fluorouridine; 5-Fluoro-2′-deoxyuridine; 1-(2-Deoxy-β-D-ribofuranosyl)-5-fluoropyrimidine-2,4(1*H*,3*H*)-dione.

Флоксуридин

$C_9H_{11}FN_2O_5$ = 246.2.

CAS — 50-91-9.



Pharmacopoeias. In *US.*

USP 31 (Floxuridine). Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Fluorouracil, p.722. Adverse reactions after intra-arterial infusion often include local reactions, thromboembolic complications, and infection or bleeding at the catheter site, or blockage of the catheter. Erythema, stomatitis, and gastrointestinal disturbances are relatively common. There have also been signs of liver dysfunction.

Effects on the liver. Serious biliary toxicity has been reported in over half of all patients receiving hepatic arterial infusions of floxuridine, usually manifesting as sclerosing cholangitis or acalculous cholecystitis;[1] as a result some surgeons routinely remove the gallbladder at the time of infusion pump implantation.[2] Extrahepatic biliary stenosis with jaundice and cholestasis has also been described;[3] the authors suggest that this could lead to intrahepatic biliary damage from bile stasis and infection, recurrent