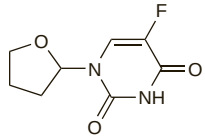
Tamoxi; ***Ital.:*** Kessar; Ledertam†; Nolvadex; Nomafen; Tamoxene; Virtamox†; ***Malaysia:*** Genox; Nolvadex; Novofen; Tamoplex; Zitazonium; ***Mex.:*** Bilem; Cryoxifeno; Fenobest; Kessar†; Nolvadex; Ralsifen-X; Tamoxan†; Taxus; Tecnofen; ***Neth.:*** Nolvadex; ***Norw.:*** Nolvadex; ***NZ:*** Genox; Nolvadex; Tamofen; ***Philipp.:*** Fenahex; Gynatam; Gyraxen; Kessar; Nolvadex; Tamoplex; Tamoxsta; Zitazonium; ***Pol.:*** Nolvadex; ***Port.:*** Mastofen; Nolvadex; Tamoxan; ***Rus.:*** Bilem (Билем)†; Tamifen (Тамифен); Zitazonium (Зитазониум); ***S.Afr.:*** Kessar; Neophedan; Nolvadex; Tamoplex; ***Singapore:*** Apo-Tamox; Nolvadex; Tamofen; ***Spain:*** Nolvadex; Sinmaren†; Yacesal; ***Swed.:*** Nolvadex; ***Switz.:*** Kessar†; Nolvadex; Tamec; ***Thai.:*** Bilem; Gynatam; Nolvadex; Novofen; Tamofen†; Tamoplex; Tuosomin; Zitazonium; ***Turk.:*** Nolvadex; Tadex; Tamofen; ***UAE:*** Tamophar; ***UK:*** Nolvadex; Soltamox; ***USA:*** Nolvadex†; Soltamox; ***Venez.:*** Gynatam; Nolvadex; Taxus.

Tegafur *(BAN, USAN, rINN)*

FT-207; Ftorafur; MJF-12264; NSC-148958; Tégafur; Tegafurum; Tegafuuri; WR-220066. 5-Fluoro-1-(tetrahydro-2-furyl)uracil; 5-Fluoro-1-(tetrahydro-2-furyl)pyrimidine-2,4(1*H*,3*H*)-dione.

Тегафур

$C_8H_9FN_2O_3$ = 200.2.
CAS — 17902-23-7.
ATC — L01BC03.
ATC Vet — QL01BC03.



Pharmacopoeias. In *Chin.* and *Jpn*.

Adverse Effects, Treatment, and Precautions

As for Fluorouracil, p.722.

Bone-marrow depression may be less severe with tegafur but gastrointestinal toxicity is often dose-limiting and central neurotoxicity is more common. Peripheral oedema and dyspnoea occur commonly. Increases in liver function test values are common and there are reports of fatal fulminant hepatitis. Liver function should be monitored in patients with hepatic impairment given tegafur; it should not be given in severe hepatic impairment.

Interactions

Tegafur should not be used with drugs that inhibit dihydropyrimidine dehydrogenase; fatalities have occurred in patients given tegafur and sorivudine (see Antivirals under Interactions of Fluorouracil, p.723). Increased plasma concentrations of phenytoin, and symptoms of toxicity during use with tegafur and uracil, have been reported.

Pharmacokinetics

Tegafur is well absorbed from the gastrointestinal tract after oral doses. After an intravenous dose it is reported to have a prolonged plasma half-life of 6 to 16 hours. Tegafur appears to be slowly metabolised in the liver to fluorouracil (p.723), and some intracellular conversion to fluorouracil may also occur. Tegafur crosses the blood-brain barrier and is found in the CSF.

◊ References.

1. Etienne-Grimaldi M-C, *et al.* A clinical pharmacokinetic analysis of tegafur-uracil (UFT) plus leucovorin given in a new twice-daily oral administration schedule. *Clin Pharmacokinet* 2007; **46:** 953–63.

Uses and Administration

Tegafur is considered to be an orally active prodrug of fluorouracil (p.723). It has been used in the management of malignant neoplasms including those of the breast, gallbladder, gastrointestinal tract, head and neck, liver, and pancreas. Tegafur has been given orally in doses up to 1 g/m^2 daily. It is often given with uracil (UFT; p.2407). Tegafur 300 mg/m^2 daily, with uracil 672 mg/m^2 daily, may be given in 3 divided oral doses, together with calcium folinate, in the management of metastatic colorectal cancer. Doses are given for a cycle of 28 days, followed by 7 days without treatment. The drugs should be taken 1 hour before or after meals, and doses modified according to toxicity. Doses of tegafur 1 to 3 g/m^2 daily for 5 days have been given intravenously.

Administration. Tegafur is an orally active prodrug of fluorouracil. Although it has been given as a single agent, it is more often used with drugs that modify its bioavailability and toxicity.[1] These include uracil (p.2407) and gimestat (5-chlorodihydropyrimidine, CDHP), which can increase fluorouracil concentrations by inhibition of dihydropyrimidine dehydrogenase, the enzyme responsible for its further catabolism,[1-3] and oxonic acid (otastat), which inhibits another enzyme, orotate pyrimidine phosphoribosyl transferase, thought to play a role in the gastrointestinal toxicity of fluorouracil and its prodrugs.[2]

UFT consists of tegafur and uracil in the optimal molar ratio 1:4.[1] It is available for the treatment of colorectal cancer (p.665)—for doses, see above. A preliminary analysis of a large study comparing oral UFT and calcium folinate therapy with intravenous fluorouracil and calcium folinate found both regimens to be well tolerated with similar levels of toxicity.[4] Adjuvant therapy with UFT appears to improve survival in patients with adenocarcinoma of the lung[5] and node-negative breast cancer.[6]

S-1 (TS-1, *Taiho Jpn*) is a combination of tegafur, gimestat and the potassium salt of oxonic acid in the molar ratio 10:4:10. It has been tried in gastric and colorectal cancers,[2,3,7,8] and initial results have suggested comparable activity to fluorouracil and calcium folinate in induction regimens, but the incidence of diarrhoea and stomatitis was reduced.

1. Adjei AA. A review of the pharmacology and clinical activity of new chemotherapy agents for the treatment of colorectal cancer. *Br J Clin Pharmacol* 1999; **48:** 265–77.
2. Sakata Y, *et al.* Late phase II study of novel oral fluoropyrimidine anticancer drug S-1 (1 M tegafur-0.4 M gimestat-1 M otastat potassium) in advanced gastric cancer patients. *Eur J Cancer* 1998; **34:** 1715–20.
3. Sugimachi K, *et al.* An early phase II study of oral S-1, a newly developed 5-fluorouracil derivative for advanced and recurrent gastrointestinal cancers. *Oncology* 1999; **57:** 202–10.
4. Smith R, *et al.* UFT plus calcium folinate vs 5-FU plus calcium folinate in colon cancer. *Oncology (Huntingt)* 1999; **13** (suppl 3): 44–7.
5. Kato H, *et al.* A randomized trial of adjuvant chemotherapy with uracil-tegafur for adenocarcinoma of the lung. *N Engl J Med* 2004; **350:** 1713–21.
6. Noguchi S, *et al.* Postoperative adjuvant therapy with tamoxifen, tegafur plus uracil, or both in women with node-negative breast cancer: a pooled analysis of six randomized controlled trials. *J Clin Oncol* 2005; **23:** 2172–84.
7. Osugi H, *et al.* Oral fluoropyrimidine anticancer drug TS-1 for gastric cancer patients with peritoneal dissemination. *Oncol Rep* 2002; **9:** 811–15.
8. Shibahara K, *et al.* Retrospective study of S-1 versus tegafur/uracil and oral leucovorin in patients with metastatic colorectal cancer. *Anticancer Res* 2008; **28:** 1779–83.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Ftorafur; UFT; ***Hong Kong:*** Futraful; ***Hung.:*** Ftorafur; ***Indon.:*** Futraful; ***Ital.:*** Citofur†; ***Jpn:*** Futraful; ***Rus.:*** Ftorafur (Фторафур); ***Spain:*** Utefos; ***Thai.:*** UFUR.

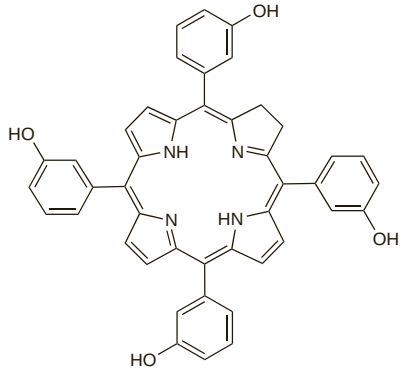
Multi-ingredient: ***Arg.:*** Asofurtal; UFT; ***Austria:*** UFT; ***Belg.:*** UFT; ***Braz.:*** UFT; ***Denm.:*** Uftoral; ***Fr.:*** UFT; ***Ger.:*** UFT; ***Gr.:*** UFT; ***Hong Kong:*** UFT; ***Hung.:*** UFT; ***Israel:*** UFT†; ***Ital.:*** UFT; ***Jpn:*** UFT; ***Malaysia:*** UFT; ***Mex.:*** UFT; ***Neth.:*** UFT; ***Norw.:*** UFT; ***NZ:*** Orzel†; ***Philipp.:*** Tefudex; UFT; ***Port.:*** UFT; ***Rus.:*** UFT (УФТ); ***S.Afr.:*** UFT; ***Singapore:*** UFT; ***Spain:*** UFT; ***Swed.:*** UFT; ***Thai.:*** UFT; ***Turk.:*** UFT; ***UK:*** Uftoral.

Temoporfin *(BAN, USAN, rINN)*

EF-9; mTHPC; Temoporfiini; Temoporfina; Témoporfine; Temoporfinum; *meso*-Tetrahydroxyphenylchlorin; *meta*-Tetrahydroxyphenylchlorin. 3,3′,3″,3‴-(7,8-Dihydroporphyrin-5,10,15,20-tetryl)tetraphenol; 7,8-Dihydro-5,10,15,20-tetrakis(3-hydroxyphenyl)porphyrin.

Темопорфин

$C_{44}H_{32}N_4O_4$ = 680.7.
CAS — 122341-38-2.
ATC — L01XD05.
ATC Vet — QL01XD05.



Adverse Effects and Precautions

Adverse effects of temoporfin include photosensitivity, local inflammatory reactions, and gastrointestinal disturbances. Patients should be advised to avoid direct sunlight or bright indoor light for 15 days, and to protect the injection site from light for at least 3 months if extravasation has occurred.

Porphyria. The use of temoporfin is contra-indicated in patients with porphyria.

Interactions

Use of temoporfin with other drugs causing photosensitivity should be avoided as the reaction may be increased; this has been reported with topical fluorouracil.

Pharmacokinetics

Peak plasma concentrations of temoporfin are reached about 2 to 4 hours after intravenous infusion. Thereafter, elimination is bi-exponential, with a terminal plasma half-life of about 65 hours. Plasma protein binding is about 85%. *Animal* data indicate that temoporfin is metabolised in the liver and excreted in the faeces via the bile.

Uses and Administration

Temoporfin is a porphyrin derivative. It is used palliatively as a photosensitiser in the photodynamic therapy (see under Porfimer Sodium, p.764) of refractory squamous cell carcinoma of the head and neck (p.666), that cannot be treated with radiotherapy, surgery, or systemic chemotherapy. It is also under investigation in the treatment of various other malignant neoplasms. Temoporfin is given by slow intravenous injection over at least 6 minutes, at a dose of 150 micrograms/kg. This is followed 96 hours later by activation using a laser tuned to a wavelength of 652 nanometres for about 200 seconds, sufficient to supply a dose of 20 J/cm^2. Treatment may be repeated once after 4 weeks if necessary.

◊ References.

1. Kubler AC, *et al.* Photodynamic therapy of primary nonmelanomatous skin tumours of the head and neck. *Lasers Surg Med* 1999; **25:** 60–8.
2. Baas P, *et al.* Photodynamic therapy with *meta*-tetrahydroxyphenylchlorin for basal cell carcinoma: a phase I/II study. *Br J Dermatol* 2001; **145:** 75–8.
3. Kubler AC, *et al.* Treatment of squamous cell carcinoma of the lip using Foscan-mediated photodynamic therapy. *Int J Oral Maxillofac Surg* 2001; **30:** 504–9.
4. Javaid B, *et al.* Photodynamic therapy (PDT) for oesophageal dysplasia and early carcinoma with mTHPC (m-tetrahydroxyphenyl chlorin): a preliminary study. *Lasers Med Sci* 2002; **17:** 51–6.
5. Friedberg JS, *et al.* A phase I study of Foscan-mediated photodynamic therapy and surgery in patients with mesothelioma. *Ann Thorac Surg* 2003; **75:** 952–9.
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7. D'Cruz AK, *et al.* mTHPC-mediated photodynamic therapy in patients with advanced, incurable head and neck cancer: a multicenter study of 128 patients. *Head Neck* 2004; **26:** 232–40.
8. Etienne J, *et al.* Photodynamic therapy with green light and mtetrahydroxyphenyl chlorin for intramucosal adenocarcinoma and high-grade dysplasia in Barrett's esophagus. *Gastrointest Endosc* 2004; **59:** 880–9. Correction. *ibid.*; **60:** 1042.
9. Hopper C, *et al.* mTHPC-mediated photodynamic therapy for early oral squamous cell carcinoma. *Int J Cancer* 2004; **111:** 138–46.
10. Lou PJ, *et al.* Interstitial photodynamic therapy as salvage treatment for recurrent head and neck cancer. *Br J Cancer* 2004; **91:** 441–6.
11. Campbell SM, *et al.* Photodynamic therapy using meta-tetrahydroxyphenylchlorin (Foscan) for the treatment of vulval intraepithelial neoplasia. *Br J Dermatol* 2004; **151:** 1076–80.
12. Naim R. Photodynamische Therapie mit m-THPC (Foscan): Behandlung von Plattenepithelkarzinomen im Kopf-Hals-Bereich. *HNO* 2008; **56:** 490–2.

Preparations

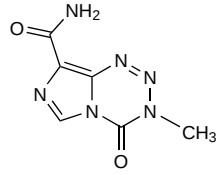
Proprietary Preparations (details are given in Part 3)
Belg.: Foscan; ***Cz.:*** Foscan; ***Denm.:*** Foscan; ***Ger.:*** Foscan; ***Gr.:*** Foscan; ***Israel:*** Foscan; ***Neth.:*** Foscan; ***Port.:*** Foscan; ***UK:*** Foscan.

Temozolomide *(BAN, USAN, rINN)*

CCRG-81045; M&B-39831; NSC-362856; Sch-52365; Temotsolomidi; Temozolomid; Temozolomida; Témozolomide; Temozolomidum. 3,4-Dihydro-3-methyl-4-oxoimidazo[5,1-*d*][1,2,-3,5]tetrazine-8-carboxamide.

Темозоломид

$C_6H_6N_6O_2$ = 194.2.
CAS — 85622-93-1.
ATC — L01AX03.
ATC Vet — QL01AX03.



Adverse Effects, Treatment, and Precautions

For general discussions see Antineoplastics, p.635, p.639, and p.641. Myelosuppression is common with temozolomide and is dose-limiting. The nadir of cell counts usually occurs 21 to 28 days after treatment, with recovery within the next 1 to 2 weeks. Patients over 70 years of age are thought to be more susceptible to severe myelosuppression. Prolonged pancytopenia may result in aplastic anaemia, and fatalities have been reported. Opportunistic infections can occur; *Pneumocystis jirovecii* pneumonia has been reported in patients