3. Ledermann JA, *et al.* Recommendation for caution with irinotecan, fluorouracil, and leucovorin for colorectal cancer. *N Engl J Med* 2001; **345:** 145–6.
4. Van Cutsem E, *et al.* Toxicity of irinotecan in patients with colorectal cancer. *N Engl J Med* 2001; **345:** 1351–2.
5. Falcone A, *et al.* Sequence effect of irinotecan and fluorouracil treatment on pharmacokinetics and toxicity in chemotherapy-naive metastatic colorectal cancer patients. *J Clin Oncol* 2001; **19:** 3456–62.

Smoking. A study found that tobacco smoking significantly affected the pharmacokinetics and toxicity of irinotecan.[1] Clearance of irinotecan was faster in smokers, and systemic exposure to the active metabolite SN-38 (see Pharmacokinetics, below) was almost 40% lower in smokers. This effect probably contributed to the significantly lower haematological toxicity seen in smokers; no significant difference in diarrhoea was seen between smokers and non-smokers. Smoking may induce cytochrome P450 isoenzyme CYP3A, or possibly affect carboxylesterase activity. The study did not determine an effect of smoking on the outcome of treatment with irinotecan. However, smokers may need a higher dose of irinotecan relative to non-smokers, since the lower exposure to irinotecan and SN-38 may indicate a potential risk of treatment failure.

1. van der Bol JM, *et al.* Cigarette smoking and irinotecan treatment: pharmacokinetic interaction and effects on neutropenia. *J Clin Oncol* 2007; **25:** 2719–26.

Thalidomide. A pharmacokinetic study found that the metabolism of irinotecan to SN-38 was significantly decreased by thalidomide. Despite reports of reduced gastrointestinal toxicity when these 2 drugs were given together (see Effects on the Gastrointestinal System, above), 3 out of 19 patients enrolled in the study had severe delayed diarrhoea after being given irinotecan with thalidomide.[1]

1. Allegrini G, *et al.* Irinotecan in combination with thalidomide in patients with advanced solid tumors: a clinical study with pharmacodynamic and pharmacokinetic evaluation. *Cancer Chemother Pharmacol* 2006; **58:** 585–93.

Pharmacokinetics

Irinotecan exhibits biphasic or triphasic pharmacokinetics, with a terminal half-life of about 14 hours. After intravenous doses it is hydrolysed by carboxylesterase in body tissues to active SN-38 (7-ethyl-10-hydroxycamptothecin). SN-38 exhibits a biphasic elimination profile with a terminal half-life of about 14 hours. Plasma protein binding for irinotecan and SN-38 is about 65% and 95%, respectively. SN-38 is mainly eliminated by glucuronidation, predominantly by the enzyme uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1). Irinotecan is also partly metabolised by cytochrome P450 isoenzymes CYP3A4 and perhaps CYP3A5. More than 50% of an intravenous dose of irinotecan is excreted as unchanged drug, with about 30% in the faeces via the bile and about 20% in the urine.

◊ References.
1. Chabot GG. Clinical pharmacokinetics of irinotecan. *Clin Pharmacokinet* 1997; **33:** 245–59.
2. Rivory LP. Metabolism of CPT-11: impact on activity. *Ann N Y Acad Sci* 2000; **922:** 205–15.
3. Mathijssen RH, *et al.* Clinical pharmacokinetics and metabolism of irinotecan (CPT-11). *Clin Cancer Res* 2001; **7:** 2182–94.
4. Ma MK, McLeod HL. Lessons learned from the irinotecan metabolic pathway. *Curr Med Chem* 2003; **10:** 41–9.
5. Smith NF, *et al.* Pharmacogenetics of irinotecan metabolism and transport: an update. *Toxicol In Vitro* 2006; **20:** 163–75.

Uses and Administration

Irinotecan is a semisynthetic derivative of the alkaloid camptothecin, obtained from the shrub *Camptotheca acuminata*. The camptothecin derivatives are inhibitors of the enzyme topoisomerase I and thus interfere with the coiling and uncoiling of DNA during replication and prevent nucleic acid synthesis. This action is specific for S phase.

Irinotecan is used, alone or with fluorouracil-based chemotherapy, in the treatment of colorectal cancer (p.665). It is also indicated for use with cetuximab in the treatment of EGFR-expressing metastatic colorectal cancer, after the failure of other regimens containing irinotecan. It has been tried in the management of other solid tumours including those of the lung (p.668).

It is given as the hydrochloride, by intravenous infusion, in at least 250 mL of glucose 5%, or sodium chloride 0.9%. In the treatment of refractory colorectal malignancies one suggested single-agent dose regimen is irinotecan hydrochloride 125 mg/m^2 infused over 90 minutes once a week for 4 weeks, followed by a 2-week rest period. Additional courses may be given if required, with doses modified according to toxicity. Another regimen requires an initial dose of 350 mg/m^2 over 30 to 90 minutes repeated every 3 weeks and adjusted according to toxicity (for dosage in hepatic impairment, see below).

For the suggestion that initial doses should be modified to reduce toxicity in those with certain genotypes, see Genetic Factors, above.

Irinotecan may also be given as part of a regimen with fluorouracil and folinic acid in the first-line treatment of metastatic colorectal cancer. Numerous regimens exist. The irinotecan hydrochloride component of the course may be given at a dose of 180 mg/m^2 over 30 to 90 minutes every 2 weeks. Alternatively, 125 mg/m^2 may be given weekly, usually on days 1, 8, 15, and 22 of a 42-day cycle. (For reference to toxicity from such regimens see under Interactions, above.)

Treatment cycles may be continued indefinitely as long as patients continue to benefit.

In the treatment of EGFR-expressing metastatic colorectal cancer, when used with cetuximab, irinotecan is given usually at the same dose as was used in the last cycles of the previous irinotecan-containing regimen; irinotecan should not be given for at least 1 hour after the end of the cetuximab infusion.

A formulation of irinotecan with hyaluronic acid is being developed.

◊ References.
1. Douillard JY, *et al.* Irinotecan combined with fluorouracil compared with fluorouracil alone as first-line treatment for metastatic colorectal cancer: a multicentre randomised trial. *Lancet* 2000; **355:** 1041–7. Correction. *ibid.*; 1372.
2. Saltz LB, *et al.* Irinotecan plus fluorouracil and leucovorin for metastatic colorectal cancer. *N Engl J Med* 2000; **343:** 905–14.
3. Rothenberg ML. Irinotecan (CPT-11): recent developments and future directions—colorectal cancer and beyond. *Oncologist* 2001; **6:** 66–80.
4. Saltz LB, *et al.* Irinotecan plus fluorouracil/leucovorin for metastatic colorectal cancer: a new survival standard. *Oncologist* 2001; **6:** 81–91.
5. Cunningham D, *et al.* Optimizing the use of irinotecan in colorectal cancer. *Oncologist* 2001; **6** (suppl 4): 17–23.
6. Vanhoefer U, *et al.* Irinotecan in the treatment of colorectal cancer: clinical overview. *J Clin Oncol* 2001; **19:** 1501–18.
7. Douillard JY, *et al.* Update on European adjuvant trials with irinotecan for colorectal cancer. *Oncology (Huntingt)* 2002; **16** (suppl 3): 13–15.
8. Ulukan H, Swaan PW. Camptothecins: a review of their chemotherapeutic potential. *Drugs* 2002; **62:** 2039–57.
9. Pizzolato JF, Saltz LB. The camptothecins. *Lancet* 2003; **361:** 2235–42.
10. Glimelius B. Benefit-risk assessment of irinotecan in advanced colorectal cancer. *Drug Safety* 2005; **28:** 417–33.
11. Fuchs C, *et al.* Irinotecan in the treatment of colorectal cancer. *Cancer Treat Rev* 2006; **32:** 491–503.
12. Sato T, *et al.* Treatment of advanced or recurrent colorectal cancer with irinotecan in Japan and elsewhere. *Expert Opin Pharmacother* 2008; **9:** 1223–8.

Administration in hepatic impairment. In patients with hyperbilirubinaemia, the clearance of irinotecan is decreased, exposure to the active metabolite SN-38 is increased, and the risk of haematological toxicity is increased. US licensed product information recommends a reduction in the initial dose of irinotecan for those patients with increased bilirubin concentrations. However, doses in patients with bilirubin greater than 2 mg/100 mL cannot be determined due to insufficient data.

In the UK, licensed product information recommends the following dosage reduction for monotherapy regimens in which irinotecan hydrochloride is normally given at 350 mg/m^2 every 3 weeks (see Uses and Administration, above):

- in patients with bilirubin up to 1.5 times the upper limit of normal range (ULN), no dosage reduction is considered necessary and irinotecan hydrochloride 350 mg/m^2 is recommended;
- in patients with bilirubin ranging from 1.5 to 3 times the ULN, irinotecan hydrochloride 200 mg/m^2 may be given;
- in patients with bilirubin over 3 times the ULN, the use of irinotecan is not recommended.

Preparations

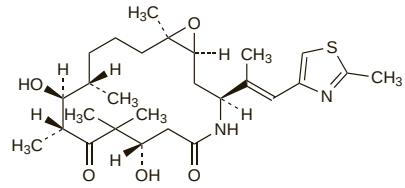
Proprietary Preparations (details are given in Part 3)
Arg.: Biotecan; Camptosar; CPT†; Efixano; Irenax; Irinogen; Itoxaril; Kebirtecan; Pipetecan; Satigene; Sibudan; Trinotecan; Winol; ***Austral.:*** Camptosar; ***Austria:*** Campto; ***Belg.:*** Campto; ***Braz.:*** Biotecan; Camptosar; Irenax; Tecnotecan; ***Canad.:*** Camptosar; ***Chile:*** Camptosar; Linatecan; ***Cz.:*** Campto; Canri; ***Denm.:*** Campto; ***Fin.:*** Campto; ***Fr.:*** Campto; ***Ger.:*** Campto; ***Gr.:*** Campto; ***Hong Kong:*** Campto; ***Hung.:*** Campto; ***India:*** Irinotel; ***Indon.:*** Campto; ***Irl.:*** Campto; ***Israel:*** Campto; ***Ital.:*** Campto; ***Malaysia:*** Campto; ***Mex.:*** Camptosar; Daritex A; Terican; ***Neth.:*** Campto; ***Norw.:*** Campto; ***NZ:*** Camptosar; ***Philipp.:*** Campto; ***Pol.:*** Campto; ***Port.:*** Campto; Faultenocan; ***Rus.:*** Campto (Кампто); Iriten (Иритен); Irnocam (Ирнокам); ***S.Afr.:*** Campto; ***Singapore:*** Campto; ***Spain:*** Campto; ***Swed.:*** Campto; ***Switz.:*** Campto; ***Thai.:*** Campto; Irinotel; ***Turk.:*** Campto; ***UK:*** Campto; ***USA:*** Camptosar; ***Venez.:*** Camptosar; Elinatecan.

Ixabepilone *(USAN, rINN)*

Azaepothilone B; BMS-247550-01; Ixabepilona; Ixabépilone; Ixabepilonum. (1*S*,3*S*,7*S*,10*R*,11*S*,12*S*,16*R*)-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[(1*E*)-1-methyl-2-(2-methylthiazol-4-yl)ethenyl]-17-oxa-4-azabicyclo[14.1.0]heptadecane-5,9-dione.

Иксабепильон

$C_{27}H_{42}N_2O_5S$ = 506.7.
CAS — 219989-84-1.
ATC — L01DC04.
ATC Vet — QL01DC04.



Adverse Effects, Treatment, and Precautions

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

Peripheral neuropathy is common with ixabepilone, and dose reduction, or delaying or stopping treatment may be necessary (see Uses and Administration, below). Dose-dependent myelosuppression can occur, manifested mainly as neutropenia; febrile neutropenia and fatalities have been reported. Frequent blood counts are recommended. Ixabepilone is formulated in polyoxyl castor oil and should be avoided in patients hypersensitive to this substance; patients should be premedicated with a histamine H_1- and histamine H_2-antagonist about 1 hour before infusion. Therapy should be stopped if a hypersensitivity reaction occurs, and symptomatic treatment given. Subsequent cycles may be given with additional corticosteroid therapy, and extension of the infusion time should be considered.

Other adverse effects include gastrointestinal disturbances, anorexia, myalgia, arthralgia, fatigue, alopecia, insomnia, headache, taste disorders, dizziness, increased lachrymation, dyspnoea, cough, skin rashes, nail disorders, palmar-plantar erythrodysesthesia syndrome, pruritus, skin exfoliation or hyperpigmentation, and hot flushes.

Interactions

Ixabepilone undergoes extensive metabolism by cytochrome P450 isoenzyme CYP3A4. Inhibitors of CYP3A4, such as ketoconazole, can increase exposure to ixabepilone. Conversely, CYP3A4 inducers can reduce exposure to ixabepilone. Use of ixabepilone with strong inhibitors or inducers of CYP3A4 should be avoided. If strong inhibitors are used, dose adjustments may be required (see Uses and Administration, below). Grapefruit juice may also increase plasma concentrations of ixabepilone and should be avoided. St John's wort may decrease plasma concentrations of ixabepilone unpredictably and should also be avoided.

Pharmacokinetics

Ixabepilone is extensively distributed. Plasma protein binding is about 67 to 77%. It is extensively metabolised in the liver, mainly by oxidation via cytochrome P450 isoenzyme CYP3A4. It is eliminated mainly as metabolites; about 86% of a dose is eliminated within 7 days, 65% in faeces, and 21% in the urine. The terminal elimination half-life is reported to be about 52 hours.

Uses and Administration

Ixabepilone is an analogue of the epothilone compound patupilone (p.761) that is used for the treatment of patients with metastatic or locally advanced breast cancer. It is given as monotherapy in those whose tumours are resistant or refractory to anthracyclines, taxanes, and capecitabine. Ixabepilone is also used with capecitabine in those whose tumours are resistant to anthracycline and taxanes, or in those with cancer resistant to taxanes, and for whom further anthracycline therapy is contraindicated.

The recommended dose of ixabepilone is 40 mg/m^2 given by intravenous infusion over 3 hours every 3 weeks. Patients with a body-surface greater than 2.2 m^2 should be dosed as calculated for 2.2 m^2. Ixabepilone is diluted with lactated Ringer's solution to a final concentration of 200 to 600 micrograms/mL before infusion.

Doses are adjusted for toxicity. If moderate or severe neuropathy, or any severe toxicity (other than neuropathy) occurs, the dose should be decreased by 20%. If severe neuropathy lasts 7 days or more, or any disabling toxicity occurs, therapy should be stopped. If the neutrophil count falls below 500 cells/mm^3 for 7 days or more, if platelets fall below 25 000 cells/mm^3 (or below 50 000 cells/mm^3 with bleeding), or if febrile neutropenia occurs, the dose should be decreased by 20%. If toxicities recur, an additional 20% dose reduction should be made. Patients should not begin a new cycle of treatment unless the neutrophil count is at least 1500 cells/mm^3, the platelet count is at least 100 000 cells/mm^3, and non-haematological toxicities have improved to grade 1 (mild) or resolved.

Doses are also adjusted in hepatic impairment (see Administration in Hepatic Impairment, below).

Use of strong inhibitors of CYP3A4 should be avoided with ixabepilone. If no alternative is available, a dose reduction of ixabepilone to 20 mg/m^2 should be considered. Once the inhibitor is stopped, a washout period of about 1 week should be allowed before the dose of ixabepilone is increased back to the original dose.

◊ References.

1. Gianni L. Ixabepilone and the narrow path to developing new cytotoxic drugs. *J Clin Oncol* 2007; **25:** 3389–91.
2. Fornier MN. Ixabepilone, first in a new class of antineoplastic agents: the natural epothilones and their analogues. *Clin Breast Cancer* 2007; **7:** 757–63.
3. Thomas ES, *et al.* Ixabepilone plus capecitabine for metastatic breast cancer progressing after anthracycline and taxane treatment. *J Clin Oncol* 2007; **25:** 5210–17.

Administration in hepatic impairment. Therapy with ixabepilone and capecitabine *combination therapy* is contra-indicated in patients with aspartate aminotransferase (AST) or alanine aminotransferase (ALT) greater than 2.5 times the upper limit of normal (ULN), or in those with bilirubin greater than the ULN. Patients with values equal to or below these figures may be given the standard dose of ixabepilone.

In *monotherapy*, the following doses of ixabepilone may be given:

- mild; AST and ALT equal to or less than 2.5 times the ULN, and bilirubin equal to or less than the ULN: 40 mg/m^2 *or* AST or ALT equal to or less than 10 times the ULN and bilirubin equal to or less than 1.5 times the ULN: 32 mg/m^2
- moderate; AST and ALT equal to or less than 10 times the ULN and bilirubin greater than 1.5 times the ULN, but equal to or less than 3 times the ULN: patients should be started at 20 mg/m^2, and the dosage in subsequent cycles escalated up to, but not exceeding, 30 mg/m^2 if tolerated
- severe; AST or ALT greater than 10 times the ULN or bilirubin greater than 3 times the ULN: not recommended

Data are limited for patients with a baseline AST or ALT greater than 5 times the ULN.

Preparations

Proprietary Preparations (details are given in Part 3)
USA: Ixempra.

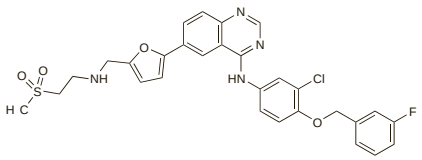
Lapatinib Tosilate *(rINNM)*

GW-572016F; Lapatinib Ditosylate *(USAN)*; Lapatinib, Tosilate de; Lapatinibi Tosilas; Tosilato de lapatinib. *N*-{3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl}-6-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)furan-2-yl]quinazolin-4-amine bis(4-methylbenzenesulfonate) monohydrate.

Лапатиниба Тозилат

$C_{29}H_{26}ClFN_4O_4S,2C_7H_8O_3S,H_2O$ = 943.5.

CAS — 231277-92-2 (lapatinib); 388082-78-8 (lapatinib tosilate).



(lapatinib)

Adverse Effects, Treatment, and Precautions

The most common adverse effects of lapatinib tosilate are gastrointestinal disturbances, dermatological reactions such as palmar-plantar erythrodysesthesia and rash, and fatigue. Diarrhoea may be severe and dose-limiting. Decreases in left ventricular ejection fraction (LVEF) have been reported with lapatinib, usually within the first 9 weeks of treatment. LVEF should be evaluated in all patients before therapy is started, and periodically evaluated during treatment. Prolongation of the QT interval has also been reported, and lapatinib should be given with caution to those patients with relevant risk factors such as hypokalaemia or hypomagnesaemia, congenital QT prolongation, use of antiarrhythmics, or cumulative high-dose anthracycline therapy. Other reported adverse effects include stomatitis, mucosal inflammation, pain in extremities, back pain, dyspnoea, and insomnia. Lapatinib should be given with caution in severe hepatic impairment; doses may need to be reduced.

Interactions

Lapatinib tosilate undergoes extensive metabolism by cytochrome P450 isoenzyme CYP3A4. Inhibitors of CYP3A4, such as ketoconazole, can increase exposure to lapatinib. Conversely, CYP3A4 inducers, such as carbamazepine, can reduce exposure to lapatinib. Use of lapatinib with strong inhibitors or inducers of CYP3A4 should be avoided; if they are to be given together, dose adjustments may be required (see Uses and Administration, below). Grapefruit juice may also increase plasma concentrations of lapatinib and should be avoided. *In vitro* studies indicate that lapatinib itself inhibits CYP3A4 and CYP2C8; it should be used cautiously with substrates of these isoenzymes that have a narrow therapeutic index.

Lapatinib is a substrate of P-glycoprotein and P-glycoprotein inhibitors can increase plasma concentrations of lapatinib. Lapatinib itself also inhibits human P-glycoprotein and may in turn increase plasma concentrations of drugs that are substrates of P-glycoprotein.

Pharmacokinetics

Absorption after an oral dose of lapatinib tosilate is variable and incomplete. Peak plasma concentrations occur after about 4 hours. Systemic exposure to lapatinib is increased when it is given with food. It is highly protein bound. Lapatinib undergoes extensive metabolism, mainly by cytochrome P450 isoenzymes CYP3A4 and CYP3A5; CYP2C19 and CYP2C8 account for some minor metabolism. The terminal half-life after a single dose has been reported to be about 14 hours; accumulation with repeated dosing indicates an effective half-life of 24 hours. About 27% and 14% of an oral dose is recovered in the faeces, as parent lapatinib and metabolites, respectively; renal excretion is negligible.

Uses and Administration

Lapatinib tosilate is a dual tyrosine kinase inhibitor directed against two members of the human epidermal growth factor receptor family, namely epidermal growth factor receptor (EGFR; ErbB1) and human epidermal receptor type 2 (HER2; ErbB2). Lapatinib is used with capecitabine (p.691) for the treatment of patients with advanced or metastatic breast cancer (p.661) whose tumours overexpress HER2, and who have had previous therapy including an anthracycline, a taxane, and trastuzumab.

Doses of lapatinib tosilate are expressed in terms of the base; lapatinib tosilate 405 mg is equivalent to about 250 mg of lapatinib.

The recommended dose of lapatinib is 1.25 g given orally once daily on days 1 to 21 of a 21-day cycle. Capecitabine is given at a dose of 2 g/m^2 daily (given orally in 2 doses about 12 hours apart) on days 1 to 14 of the cycle. Treatment may be continued until disease progression or unacceptable toxicity occurs. If a daily dose is missed, the next day's dose should not be doubled. Lapatinib is given at least one hour before or one hour after food.

Dosage should be reduced in patients with severe hepatic impairment (see Administration in Hepatic Impairment, below). Treatment with lapatinib should be stopped in patients who develop a decreased left ventricular ejection fraction (LVEF); however, patients may be restarted at a reduced dose of lapatinib 1 g daily after a minimum of 2 weeks if the LVEF recovers to normal and if the patient is asymptomatic. Lapatinib may need to be stopped or treatment interrupted if other severe toxicities develop. Patients can be restarted at the recommended dose when the toxicity improves. However, if toxicity recurs, lapatinib should be restarted at the lower dose of 1 g daily.

If use with potent inhibitors or inducers of cytochrome P450 isoenzyme CYP3A4 cannot be avoided, dose adjustments of lapatinib are considered necessary, based on pharmacokinetic studies. Lapatinib should be given at a dose of 500 mg daily when given with a potent CYP3A4 inhibitor; if the inhibitor is stopped, a washout period of about 1 week should be allowed before the lapatinib dose is increased to the usual recommended dose. When given with a potent inducer of this isoenzyme, the dose of lapatinib should be titrated gradually from 1.25 g daily up to 4.5 g daily, based on tolerability; if the inducer is stopped, the dose of lapatinib should be reduced to the usual recommended dose.

Lapatinib is also under investigation for the treatment of head and neck squamous cell carcinoma.

◊ References.

1. Nelson MH, Dolder CR. Lapatinib: a novel dual tyrosine kinase inhibitor with activity in solid tumors. *Ann Pharmacother* 2006; **40:** 261–9.
2. Moy B, Goss PE. Lapatinib: current status and future directions in breast cancer. *Oncologist* 2006; **11:** 1047–57.
3. Geyer CE, *et al.* Lapatinib plus capecitabine for HER2-positive advanced breast cancer. *N Engl J Med* 2006; **355:** 2733–43.
4. Montemurro F, *et al.* Lapatinib: a dual inhibitor of EGFR and HER2 tyrosine kinase activity. *Expert Opin Biol Ther* 2007; **7:** 257–68.
5. Ito Y, *et al.* Does lapatinib, a small-molecule tyrosine kinase inhibitor, constitute a breakthrough in the treatment of breast cancer? *Breast Cancer* 2007; **14:** 156–62.
6. Dhillon S, Wagstaff AJ. Lapatinib. *Drugs* 2007; **67:** 2101–8.

Administration in hepatic impairment. Systemic exposure to lapatinib after a single 100-mg oral dose increased by about 14% and 63% in subjects with moderate (Child-Pugh Class B) and severe (Child-Pugh Class C) hepatic impairment, when compared with healthy control subjects. Caution is advised when lapatinib is given to patients with severe hepatic impairment. Oral doses should be reduced to 750 mg daily. However, licensed product information warns that there are no clinical data with this dose adjustment in patients with severe hepatic impairment.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Tykerb; ***Fr.:*** Tyverb; ***Switz.:*** Tyverb; ***UK:*** Tyverb; ***USA:*** Tykerb.

Lenalidomide *(BAN, USAN, rINN)*

CC-5013; CDC-501; Lénalidomide; Lenalidomidum. 3-(4-Amino-1-oxo-1,3-dihydro-2*H*-isoindol-2-yl)piperidine-2,6-dione.

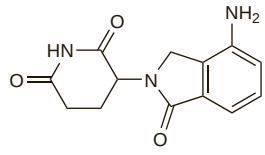
Леналидомид

$C_{13}H_{13}N_3O_3$ = 259.3.

CAS — 191732-72-6.

ATC — L04AX04.

ATC Vet — QL04AX04.



Adverse Effects, Treatment, and Precautions

Lenalidomide is associated with significant neutropenia and thrombocytopenia. Anaemia is also common. Patients may require dose reduction or therapy may need to be delayed or stopped. Full blood counts should be monitored weekly for the first 8 weeks of therapy, and monthly thereafter. There is also an increased risk of deep-vein thrombosis and pulmonary embolism with lenalidomide. Other adverse effects include gastrointestinal disturbances, pruritus, rash, and fatigue. Dyspnoea, muscle cramps, hypotension, tremor, hypoaesthesia, and infections such as pneumonia are common. Peripheral neuropathy has been reported, as have cases of hypothyroidism; thyroid function should be monitored. Cardiac disorders and hepatotoxicity have also been reported. Caution is advised in patients with renal impairment as lenalidomide is excreted via the kidneys.