Viessia; Vinilex; ***Neth.:*** Navelbine; ***Norw.:*** Navelbine; ***NZ:*** Navelbine; ***Philipp.:*** Navelbine; Vinotel; ***Pol.:*** Navelbine; Navirel; ***Port.:*** Navelbine; Vinorel; ***Rus.:*** Maverex (Маверекс); Navelbine (Навельбин); ***S.Afr.:*** Navelbine; ***Singapore:*** Navelbine; ***Spain:*** Navelbine; ***Swed.:*** Navelbine; ***Switz.:*** Navelbine; ***Thai.:*** Navelbine; Vinelbine; ***Turk.:*** Navelbine; ***UK:*** Navelbine; ***USA:*** Navelbine.

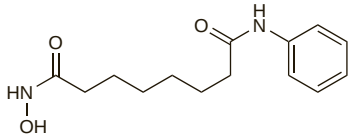
Vorinostat *(USAN, rINN)*

SAHA; Suberoylanilide Hydroxamic Acid; Vorinostatum. *N*-Hydroxy-*N*′-phenyl octanediamide.

Вориностат

$C_{14}H_{20}N_2O_3$ = 264.3.

CAS — 149647-78-9.



Adverse Effects, Treatment, and Precautions

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

The most common adverse effects of vorinostat are gastrointestinal disturbances, fatigue, chills, dry mouth and taste disorders. Thrombocytopenia and anaemia also occur commonly, and are dose-related; dose reductions may be necessary and in some instances, therapy may need to be stopped. Pulmonary embolism has occurred. Other adverse effects include muscle spasms, alopecia, dizziness, peripheral oedema, headache, pruritus, cough, upper respiratory-tract infection, and pyrexia. Hypokalaemia and hyperglycaemia have been reported, as has prolongation of the QT interval. Blood cell counts, electrolytes, glucose, and serum creatinine should be monitored every 2 weeks during the first 2 months of therapy and monthly thereafter. Baseline and periodic ECG monitoring should be performed.

Interactions

Severe thrombocytopenia and gastrointestinal bleeding have been reported when vorinostat has been given with other histone deacetylase inhibitors such as valproic acid; platelet counts should be monitored every 2 weeks for the first 2 months of therapy. Vorinostat may prolong prothrombin time and affect the INR in patients receiving coumarin anticoagulants.

Pharmacokinetics

After an oral dose of vorinostat with a high-fat meal, mean time to maximum plasma concentration was about 4 hours; this was reduced to 1.5 hours after fasting. Aside from this decrease in the rate of absorption, a high-fat meal also increased the extent of absorption. While these results were stated not to be clinically significant, licensed product information recommends that vorinostat be taken with food. Plasma protein binding is about 71%. Vorinostat is metabolised by glucuronidation and hydrolysis followed by oxidation; metabolites are pharmacologically inactive. Less than 1% of a dose is recovered in the urine as unchanged drug. The mean terminal half-life is about 2 hours for vorinostat.

◊ References.

1. Rubin EH, *et al.* A study to determine the effects of food and multiple dosing on the pharmacokinetics of vorinostat given orally to patients with advanced cancer. *Clin Cancer Res* 2006; **12:** 7039–45.

Uses and Administration

Vorinostat is a histone deacetylase inhibitor used for the treatment of cutaneous T-cell lymphoma (see Non-Hodgkin's Lymphomas, p.656). The recommended dose is 400 mg orally, given once daily with food. This may be reduced to 300 mg once daily, with a further reduction to 300 mg once daily for 5 consecutive days of each week, if needed. Treatment may be continued as long as there is no evidence of progressive disease or unacceptable toxicity.

Vorinostat is also under investigation for the treatment of multiple myeloma and mesothelioma.

◊ References.

1. O'Connor OA. Clinical experience with intravenous and oral formulations of the novel histone deacetylase inhibitor suberoylanilide hydroxamic acid in patients with advanced hematologic malignancies. *J Clin Oncol* 2006; **24:** 166–73.
2. Krug LM, *et al.* Potential role of histone deacetylase inhibitors in mesothelioma: clinical experience with suberoylanilide hydroxamic acid. *Clin Lung Cancer* 2006; **7:** 257–61.
3. Richon VM. Cancer biology: mechanism of antitumour action of vorinostat (suberoylanilide hydroxamic acid), a novel histone deacetylase inhibitor. *Br J Cancer* 2006; **95** (suppl): S2–S6.
4. O'Connor OA. Clinical experience with the novel histone deacetylase inhibitor vorinostat (suberoylanilide hydroxamic acid) in patients with relapsed lymphoma. *Br J Cancer* 2006; **95** (suppl): S7–S12.
5. Duvic M, Zhang C. Clinical and laboratory experience of vorinostat (suberoylanilide hydroxamic acid) in the treatment of cutaneous T-cell lymphoma. *Br J Cancer* 2006; **95** (suppl): S13–S19.
6. Anonymous. Vorinostat (Zolinza) for cutaneous T-Cell lymphoma. *Med Lett Drugs Ther* 2007; **49:** 23–4.

Preparations

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

Vorozole *(BAN, USAN, rINN)* ⊗

R-83842; Vorozol; Vorozolum. (+)-6-[4-Chloro-α-(1,2,4-triazol-1-yl)benzyl]-1-methyl-1*H*-benzotriazole.

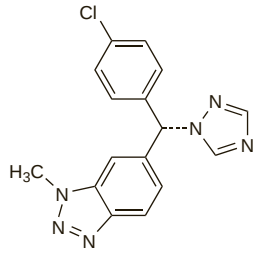
Ворозол

$C_{16}H_{13}ClN_6$ = 324.8.

CAS — 129731-10-8.

ATC — L02BG05.

ATC Vet — QL02BG05.



Profile

Vorozole is a selective nonsteroidal inhibitor of the aromatase (oestrogen synthetase) system. It has been investigated in the treatment of breast cancer.

◊ References.

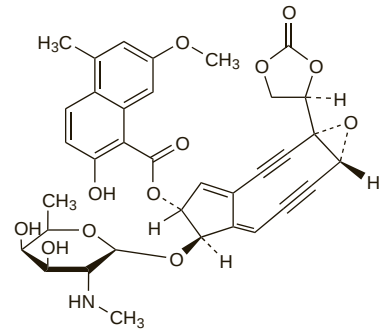
1. Goss PE, *et al.* Randomized phase III trial comparing the new potent and selective third-generation aromatase inhibitor vorozole with megestrol acetate in postmenopausal advanced breast cancer patients. *J Clin Oncol* 1999; **17:** 52–63.
2. Harper-Wynne CL, *et al.* Comparison of the systemic and intratumoral effects of tamoxifen and the aromatase inhibitor vorozole in postmenopausal patients with primary breast cancer. *J Clin Oncol* 2002; **20:** 1026–35.

Zinostatin *(USAN, rINN)*

Neocarzinostatin; NSC-69856; NSC-157365; Zinostatina; Zinostatine; Zinostatinum.

Зиностатин

CAS — 9014-02-2.



Description. Zinostatin is an antineoplastic antibiotic obtained from *Streptomyces carzinostaticus.*

Pharmacopoeias. *Jpn* includes zinostatin stimalamer.

Profile

Zinostatin is an antibiotic with antineoplastic activity and has been used in the treatment of malignant neoplasms.

Zinostatin stimalamer (SMANCS), a conjugate of zinostatin with a styrene-maleic acid polymer, is used for the treatment of liver cancer.

Zorubicin Hydrochloride *(USAN, rINNM)*

Hidrocloruro de zorubicina; NSC-164011; RP-22050 (zorubicin); Zorubicine, Chlorhydrate de; Zorubicini Hydrochloridum. Benzoic acid (2*S*-*cis*)-{1-[4-(3-amino-2,3,6-trideoxy-α-L-*lyxo*-hexopyranosyloxy)-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxonaphthacen-2-yl]ethylidene}hydrazide hydrochloride.

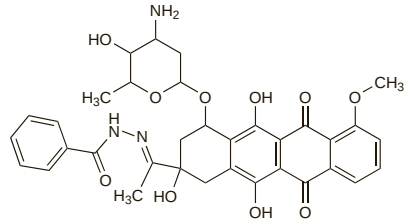
Зорубицина Гидрохлорид

$C_{34}H_{35}N_3O_{10}$,HCl = 682.1.

CAS — 54083-22-6 (zorubicin); 36508-71-1 (zorubicin hydrochloride).

ATC — L01DB05.

ATC Vet — QL01DB05.



(zorubicin)

Profile

Zorubicin is an anthracycline antibiotic with antineoplastic actions similar to those of doxorubicin (see p.712). It has been used as the hydrochloride in the treatment of acute leukaemias.