

Product Data Sheet

Product Name: Epothilone D

Cat. No.: GC17440

Chemical Properties

Cas. No. 189453-10-9

Chemical Name (4S,7R,8S,9S,13Z,16S)-4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(E)-1-(2-methyl-1,3-thiazol-4-yl)prop-1-en-2-yl]-1-oxacyclohexadec-13-ene-2,6-dione

SMILES CC1CCCC(=CCC(OC(=O)CC(C(C(=O)C(C1O)C)(C)C)O)C(=CC2=CSC(=N2)C)C)C

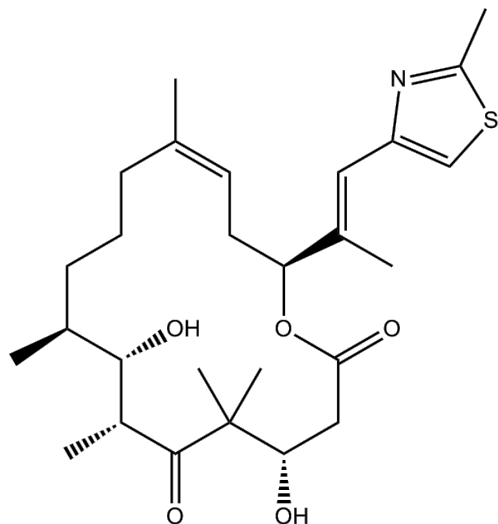
Formula $C_{27}H_{41}NO_5S$ M.Wt 491.68

Solubility DMSO : ≥ 100 mg/mL (203.38 mM) Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

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**Animal
experiment:**

Mice[2] Groups of mice (n=3) receive intraperitoneal (i.p.) injections of 3.7 mg/kg of Epothilone D (epoD) dissolved in 100% DMSO, followed by euthanization using approved at times ranging from 0.25 h to 24 h. In another study, groups of mice (n=3) receive injections of 3 mg/kg of epoD in 100% DMSO followed by euthanization 4, 6 and 10 days later. The Epothilone D (epoD) levels in brain and blood samples are determined using LC-MS/MS protocols. Groups (n=10-13) of 3-month old PS19 tau Tg mice or 3-month old non-Tg littermates are administered weekly i.p. injections of 1 mg/kg epoD, 3 mg/kg of Epothilone D (epoD) or vehicle (DMSO), for a total of 3 months. Animals are monitored for signs of abnormal behavior or distress, and are weighed weekly. After final dosing, the mice undergo motor function and cognitive testing. After euthanization, brains and optic nerve (ON) are recovered for immunohistochemical analyses. A subset of mice from each group also undergo necropsy evaluation with organ weights recorded.

References:

- [1]. Konner J, et al. Phase I clinical, pharmacokinetic, and pharmacodynamic study of KOS-862 (Epothilone D) in patients with advanced solid tumors and lymphoma. Invest New Drugs. 2012 Dec;30(6):2294-302.
- [2]. Brunden KR, et al. Epothilone D improves microtubule density, axonal integrity, and cognition in a transgenic mouse model of tauopathy. J Neurosci. 2010 Oct 13;30(41):13861-6.

Background

IC50: 2.9 nM for MCF-7 cell line; 2.7 nM for KB-31 cell line; 9.5 nM for CCRF-CEM cell line

Drugs targeting tubulin are active in human malignant disease and are an essential component of medical treatment of these diseases. As a result, pharmaceutical research on compounds that interfere with tubulin function has concentrated on agents which might have enhanced efficacy or reduced toxicity. Epothilone D is a more potent microtubule stabilizer.

In vitro: Epothilone D is a more potent microtubule stabilizer in vitro than epothilone A or B. In vitro,

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Epothilone D showed potent cytotoxicity in a panel of human tumor cell lines, with similar potency to paclitaxel. It also showed definite advantage over paclitaxel in drug-resistant cell lines, and retained its cytotoxicity against a multidrug resistant cell line over-expressing P-glycoprotein [1].

In vivo: In vivo, antitumor efficacy of Epothilone D has been observed in both paclitaxel sensitive and resistant xenografts, as well as certain multidrug resistant xenografts including a doxorubinresistant CCRF-CEM leukemic cell xenograft [1].

Clinical trial: Epothilone D was well tolerated with manageable toxicity, favorable PK profile, and clinical activity. The maximum tolerated dose was determined to be 100 mg/m² weekly 3-on/1-off. MTBF can be demonstrated in PBMCs of patients exposed to Epothilone D [1].

Reference:

[1] Konner J, Grisham RN, Park J, O'Connor OA, Cropp G, Johnson R, Hannah AL, Hensley ML, Sabbatini P, Mironov S, Danishefsky S, Hyman D, Spriggs DR, Dupont J, Aghajanian C. Phase I clinical, pharmacokinetic, and pharmacodynamic study of KOS-862 (Epothilone D) in patients with advanced solid tumors and lymphoma. Invest New Drugs. 2012 Dec;30(6):2294-302. doi: 10.1007/s10637-011-9765-7.

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