Namitecan

Cat. No.: HY-14821

CAS No.: 372105-27-6

Molecular Formula: $C_{23}H_{22}N_4O_5$

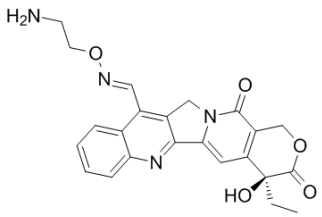
Molecular Weight: 434.44

Target: Topoisomerase

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (575.45 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3018 mL	11.5091 mL	23.0181 mL
5 mM	0.4604 mL	2.3018 mL	4.6036 mL
10 mM	0.2302 mL	1.1509 mL	2.3018 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.79 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.79 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Namitecan is a potent topoisomerase I inhibitor, with antitumor property.

IC_{50} & Target

Topoisomerase I

In Vitro

Namitecan and cetuximab cooperate in inhibiting EGFR expression. Namitecan induces a dose-dependent decrease in EGFR expression in the different cell lines[1]. ST1968 induces a comparable level of apoptosis in A431 and A431/TPT cells with IC_{50} of 0.21 and 0.29 μM[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Namitecan (10 mg/kg) in combination with cetuximab (1 mg/mouse) induces synergistic antitumor effects in SCC models as

a function of EGFR gene copy number[1]. ST1968 (25 mg/kg) causes acceptable body weight loss and no toxic deaths. ST1968 produces a 100% complete response rate in the mice bearing the A431 tumor, and retains a relevant activity in the topotecan-resistant tumor[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]

The antiproliferative activity is evaluated after 72 hours of drug exposure by cell counting. Drug concentrations able to inhibit cell proliferation by 50% (IC_{50}) and 20% (IC_{20}) are calculated from dose-response curves.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [1]

To generate tumor xenografts, exponentially growing cells (A431 and A431/topotecan, 10^7 cells/mouse; SiHa 2.5×10^7 cells/mouse, Caski 10^7 cells/mouse) are s.c. injected into the mice flanks. For antitumor activity studies, groups of four/five mice bearing tumor implanted in both flanks are used. Tumor fragments are implanted on day 0, and tumor growth is followed by biweekly measurements of tumor diameters with a Vernier caliper. Tumor volume (TV) is calculated according to the formula TV (mm^3) = $d^2 \times D/2$, in which d and D are the shortest and the longest diameter, respectively. Treatment starts 5 to 13 days after implant, when the tumors are just palpable, but established (TV = 80-90 mm^3). Namitecan, irinotecan, and cetuximab are administered every fourth day for four times. Cetuximab is given 1 hour after each administration of the camptothecin.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. De Cesare M, et al. Synergistic antitumor activity of cetuximab and namitecan in human squamous cell carcinoma models relies on cooperative inhibition of EGFR expression and depends on high EGFR gene copy number. Clin Cancer Res. 2014 Feb 15;20(4):995-1006.

[2]. Zuco V, et al. Efficacy of ST1968 (namitecan) on a topotecan-resistant squamous cell carcinoma. Biochem Pharmacol. 2010 Feb 15;79(4):535-41.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA