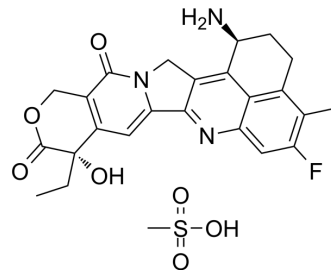


## Exatecan mesylate

<b>Cat. No.:</b>	HY-13631A
<b>CAS No.:</b>	169869-90-3
<b>Molecular Formula:</b>	C <sub>25</sub> H <sub>26</sub> FN <sub>3</sub> O <sub>7</sub> S
<b>Molecular Weight:</b>	531.55
<b>Target:</b>	Topoisomerase; ADC Cytotoxin
<b>Pathway:</b>	Cell Cycle/DNA Damage; Antibody-drug Conjugate/ADC Related
<b>Storage:</b>	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 1 years; -20°C, 6 months (sealed storage, away from moisture and light)



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : 15 mg/mL (28.22 mM; Need ultrasonic)  
H<sub>2</sub>O : < 0.1 mg/mL (ultrasonic;warming;heat to 80°C) (insoluble)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	1.8813 mL	9.4065 mL	18.8129 mL
	5 mM	0.3763 mL	1.8813 mL	3.7626 mL
	10 mM	0.1881 mL	0.9406 mL	1.8813 mL

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

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 1.25 mg/mL (2.35 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 0.67 mg/mL (1.26 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 0.67 mg/mL (1.26 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

Exatecan mesylate (DX8951f) is a DNA topoisomerase I inhibitor, with an IC<sub>50</sub> of 2.2 μM (0.975 μg/mL). Exatecan mesylate can be used in cancer research.

#### IC<sub>50</sub> & Target

Topoisomerase I  
0.975 μg/mL (IC<sub>50</sub>)

#### In Vitro

Exatecan mesylate is a potent topoisomerase I inhibitor, with an IC<sub>50</sub> of 0.975 μg/mL. Exatecan mesylate (DX-8951f)

significantly inhibits the proliferation of several cancer cell lines, with mean GI<sub>50</sub>s of 2.02 ng/mL, 2.92 ng/mL, 1.53 ng/mL, and 0.877 ng/mL for breast cancer cells, colon cancer cells, stomach cancer cells and lung cancer cells, respectively<sup>[1]</sup>. Exatecan mesylate (DX-8951f) displays cytotoxic activities against PC-6, PC-6/SN2-5 cells, with mean GI<sub>50</sub>s of 0.186 and 0.395 ng/mL, respectively. Exatecan mesylate (34 nM) stabilizes DNA-TopoI complexes in PC-6 and PC-6/SN2-5 cells<sup>[3]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

Exatecan mesylate (DX-8951f, 3.325-50 mg/kg, i.v.) exhibits antitumor activities in the mice model bearing tumor cells, without toxic death<sup>[1]</sup>. Exatecan mesylate (15, 25 mg/kg, i.v.) highly inhibits MIA-PaCa, BxPC-3 primary tumor growth in the MIA-PaCa-2 early-stage model and early-stage model of BxPC-3. Exatecan mesylate (15, 25 mg/kg, i.v.) also significantly suppresses BxPC-3 lymphatic metastasis and completely eliminates lung metastasis in the BxPC-3 late-stage cancer model<sup>[2]</sup>.

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

## PROTOCOL

#### Kinase Assay<sup>[3]</sup>

Cells ( $5 \times 10^6$ ) are lysed with SDS buffer (10 mM HEPES, 2 mM orthovanadate, 10 mM NaF, 10 mM pyrophosphate, 1 mM PMSF, 10 µg/mL leupeptin, 10% 2-mercaptoethanol, 10% glycerol, 8% SDS, 42 mM Tris-HCl, 0.002% bromophenol blue, pH 7.4). Protein in the whole cell lysates is separated in 7.5% polyacrylamide gel and blotted onto nitrocellulose membrane. The membrane is treated with anti-Topo I human antibody and subsequently, with horseradish peroxidase-conjugated protein A. The Topo I-specific band is detected with ECL reagents. To obtain a nuclear extract, cells ( $5 \times 10^7$ ) are washed with ice-cold buffer (2 mM K<sub>2</sub>HPO<sub>4</sub>, 5 mM MgCl<sub>2</sub>, 150 mM NaCl, 1 mM EGTA, 0.1 mM dithiothreitol), resuspended in buffer containing 0.35% Triton-X100 and PMSF and then incubated on ice for 10 min. The resulting lysates are centrifuged, and precipitates are then incubated with buffer containing 0.35 M NaCl for 1 hr at 4°C. After centrifugation (18,000g, 10 min), the protein concentration of the supernatant (nuclear extract) is determined using a protein assay kit. The same amount of nuclear protein is analyzed by Western blotting analysis using anti-Topo I antibody<sup>[3]</sup>.

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#### Cell Assay<sup>[1]</sup>

Growth inhibition experiments are carried out in 96-well flat-bottomed microplates, and the amount of viable cell at the end of the incubation is determined by MTT assay. Thus, 500-20000 cells/well in 150 µL of medium are plated and grown for 24 h (P388, CCRF-CEM and K562 cells for 4h), the drug (including Exatecan Mesylate, in 150 µL medium/well), or the medium alone as a control, is added, and the cells are cultured for an additional 3 days. After addition of MTT (20 µL/well, 5 mg/mL in phosphate-buffered saline), the plates are incubated for 4 h and centrifuged at 800 g for 5 min, then the medium is removed and the blue dye formed is dissolved in 150 µL of DMSO. The absorbance is measured at 540 nm using a Microplate Reader model 3550<sup>[1]</sup>.

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#### Animal Administration<sup>[2]</sup>

At 3 weeks after BxPC-3-GFP and MIA-PaCa-2-GFP orthotopic implantation, mice are randomized into five different groups of 5 mice each for treatment purposes. Group 1 serves as the negative control and does not receive any treatment. Groups 2 and 3 are treated with Exatecan Mesylate at 25 and 15 mg/kg/dose, respectively. Groups 4 and 5 receive LY 188011 treatments at 300 and 150 mg/kg/dose, respectively. At 6 weeks after BxPC-3-GFP orthotopic implantation, mice are randomized into three different groups of 20 mice each for treatment purposes. Group 1 serves as the negative control and does not receive any treatment. Group 2 is treated with 25 mg/kg/dose Exatecan Mesylate and group 3 receives 300 mg/kg/dose LY 188011. Dosing for both drugs is performed once a week for 3 weeks, discontinued for 2 weeks, and then continued for another 3 weeks. In both early and late cancer models, primary tumor size and body weights are measured once a week. Tumor volumes are calculated using the formula  $a \times b^2 \times 0.5$ , where a and b represent the larger and smaller diameters, respectively. At the termination of the studies, mice are sacrificed and explored. Final tumor weights and direct GFP images of primary tumor and metastases are recorded for each mouse. The tumor growth IR is calculated using the formula  $IR (\%) = (1 - TWt/TWc) \times 100$ , where TWt and TWc are the mean tumor weight of treated and control groups, respectively<sup>[2]</sup>.

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## CUSTOMER VALIDATION

- Mol Cancer Ther. 2023 Sep 5;22(9):1013-1027.
- Mol Pharm. 2022 Dec 2.
- Pharmaceuticals. 2021, 14(3), 247.
- Patent. US20220162323A1.
- Patent. US20210009719A1.

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## REFERENCES

[1]. Mitsui I, et al. A new water-soluble camptothecin derivative, DX-8951f, exhibits potent antitumor activity against human tumors in vitro and in vivo. Jpn J Cancer Res. 1995 Aug;86(8):776-82.

[2]. Sun FX, et al. Efficacy of camptothecin analog DX-8951f (Exatecan Mesylate) on human pancreatic cancer in an orthotopic metastatic model. Cancer Res. 2003 Jan 1;63(1):80-5.

[3]. Joto N, et al. DX-8951f, a water-soluble camptothecin analog, exhibits potent antitumor activity against a human lung cancer cell line and its SN-38-resistant variant. Int J Cancer. 1997 Aug 7;72(4):680-6.

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

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