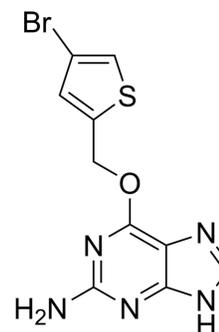


## Lomeguatrib

<b>Cat. No.:</b>	HY-13668		
<b>CAS No.:</b>	192441-08-0		
<b>Molecular Formula:</b>	C <sub>10</sub> H <sub>8</sub> BrN <sub>5</sub> OS		
<b>Molecular Weight:</b>	326.17		
<b>Target:</b>	DNA Methyltransferase		
<b>Pathway:</b>	Epigenetics		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 56 mg/mL (171.69 mM)  
 \* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent	Mass	1 mg	5 mg	10 mg
	Concentration				
	1 mM		3.0659 mL	15.3294 mL	30.6589 mL
	5 mM		0.6132 mL	3.0659 mL	6.1318 mL
	10 mM		0.3066 mL	1.5329 mL	3.0659 mL

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

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
 Solubility: ≥ 2.08 mg/mL (6.38 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
 Solubility: ≥ 2.08 mg/mL (6.38 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
 Solubility: ≥ 2.08 mg/mL (6.38 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

Lomeguatrib is a O<sup>6</sup>-methylguanine-DNA methyltransferase (MGMT) inhibitor, with IC<sub>50</sub>s of 9 nM in cell-free assay and -6 nM in MCF-7 cells.

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

MGMT	MGMT
6 nM (IC <sub>50</sub> , in MCF-7 cells)	9 nM (IC <sub>50</sub> )

<b>In Vitro</b>	<p>Lomeguatrib (Compound 10) is a O<sup>6</sup>-methylguanine methyltransferase (MGMT) inhibitor, with an IC<sub>50</sub> of 9 nM in cell-free assay<sup>[1]</sup> and -6 nM in MCF-7 cells. Lomeguatrib (10 μM) substantially increases the growth inhibitory effects of temozolomide in MCF-7 cells (D<sub>60</sub>=10 μM with Lomeguatrib vs 400 μM without)<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>In Vivo</b>	<p>Lomeguatrib (20 mg/kg i.p.) completely inactivates MGMT within 2 h, but shows no significant effect on tumor growth in MCF-7 xenografts<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## PROTOCOL

<b>Kinase Assay</b> <sup>[1]</sup>	<p>Briefly, 200 μg of extracted cellular protein from HeLaS3 cells in 200 μL of 70 mM HEPES buffer (with 1 mM dithiothreitol (DTT), 5 mM EDTA, pH 7.8) is incubated at 37°C with a defined concentration of Lomeguatrib (added as a DMSO solution). After 30 min an excess of [<sup>3</sup>H]-methylated DNA (120 000 cpm) is added, and the incubation is continued for an additional 90 min. The reaction is stopped by the addition of 400 μL TCA (13%), and the DNA is hydrolyzed by heating the reaction mixture for 30 min at 98°C. The precipitated protein is washed three times with 400-μL portions of 5% TCA, solubilized in 0.1 N NaOH, and analyzed by liquid scintillation counting using the cocktail Rotiszint eco plus and a TRI-CARB. Enzyme activity is expressed as fmol of [<sup>3</sup>H]methyl transferred to TCA-insoluble protein material per mg of total cellular protein. Percent inhibition is calculated relative to untreated control samples. Each assay is repeated three times, and IC<sub>50</sub> values are determined graphically from plots of percent inhibition vs inhibitor concentration<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>Cell Assay</b> <sup>[2]</sup>	<p>To determine toxicity, the MTT growth inhibition assay is employed. Cells (1000 per well) are plated into a 96-well plate and following a 24 h attachment period, Lomeguatrib is added to the cells. After 2 h incubation with Lomeguatrib (10 μM) at 37°C, 5% CO<sub>2</sub>, increasing doses of temozolomide or vehicle are added and the cells are incubated for a further 4-5 days. At the end of the exposure period, 150 μg MTT is added to each well and plates are incubated for 3 h at 37°C, 5% CO<sub>2</sub>. The media are removed and the formazan crystals formed in the viable cells are solubilised in 200 μL DMSO. The absorbances at 540 and 690 nm are determined using a ELISA plate reader and growth inhibition calculated as a percentage of the A540-A690 of untreated wells<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>Animal Administration</b> <sup>[2]</sup>	<p>Mice<sup>[2]</sup></p> <p>To assess the ability of Lomeguatrib to sensitise human breast tumour xenografts to the tumour growth inhibitory effects of temozolomide, groups of at least six nude mice are treated as follows: the vehicle control group are given corn oil then 20% DMSO in PBS; the temozolomide only group are given corn oil then temozolomide (100 mg/kg/day); the Lomeguatrib only group are given Lomeguatrib (20 mg/kg/day) then DMSO in PBS, and the Lomeguatrib plus temozolomide group are given Lomeguatrib (20 mg/kg/day) then temozolomide (100 mg/kg/day). Drugs or vehicles are administered i.p. once daily for 5 days with a separation of 1 h. Up to 10 and at least six animals are assigned to each group, and mean tumour volume is standardised across the groups at the start of the experiment: thus the control, Lomeguatrib, temozolomide and Lomeguatrib plus temozolomide groups had mean tumour volumes of 29.8±7.6 (range 19.0-38.7), 33.2±14.7 (range 16.5-58.7), 35.1±10.9 (range 20.9-52.4) and 30.3±10.0 (range 20.7-44.5) mm<sup>3</sup>, respectively<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.
- Oncogene. 2021 Apr;40(15):2711-2724.
- CNS Neurosci Ther. 2021 Jan 18.

- Molecules. 2022, 27(19), 6219.
- Preprints. 2021, 2021060097.

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## REFERENCES

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- [1]. Reinhard J, et al. Monosaccharide-linked inhibitors of O(6)-methylguanine-DNA methyltransferase (MGMT): synthesis, molecular modeling, and structure-activity relationships. J Med Chem. 2001 Nov 22;44(24):4050-61.
- [2]. Clemons M, et al. O6-(4-bromothenyl)guanine reverses temozolomide resistance in human breast tumour MCF-7 cells and xenografts. Br J Cancer. 2005 Nov 14;93(10):1152-6.
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**Caution: Product has not been fully validated for medical applications. For research use only.**

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: [tech@MedChemExpress.com](mailto:tech@MedChemExpress.com)

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