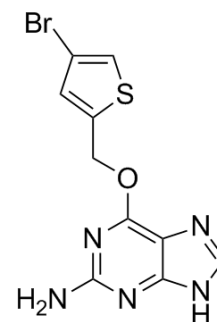


Lomeguatrib

| | | | |
|---------------------------|--|-------|----------|
| Cat. No.: | HY-13668 | | |
| CAS No.: | 192441-08-0 | | |
| Molecular Formula: | C ₁₀ H ₈ BrN ₅ OS | | |
| Molecular Weight: | 326.17 | | |
| Target: | DNA Methyltransferase | | |
| Pathway: | Epigenetics | | |
| 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 : ≥ 56 mg/mL (171.69 mM)
 * "≥" means soluble, but saturation unknown.

| Preparing Stock Solutions | Solvent | | Mass | | |
|---------------------------|---------------|--|-----------|------------|------------|
| | Concentration | | 1 mg | 5 mg | 10 mg |
| | 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 O⁶-methylguanine-DNA methyltransferase (MGMT) inhibitor, with IC₅₀s of 9 nM in cell-free assay and -6 nM in MCF-7 cells.

IC₅₀ & Target

| | |
|--|--------------------------|
| MGMT | MGMT |
| 6 nM (IC ₅₀ , in MCF-7 cells) | 9 nM (IC ₅₀) |

| | |
|-----------------|---|
| In Vitro | <p>Lomeguatrib (Compound 10) is a O⁶-methylguanine methyltransferase (MGMT) inhibitor, with an IC₅₀ of 9 nM in cell-free assay^[1] and -6 nM in MCF-7 cells. Lomeguatrib (10 μM) substantially increases the growth inhibitory effects of temozolomide in MCF-7 cells (D₆₀=10 μM with Lomeguatrib vs 400 μM without)^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> |
| In Vivo | <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^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> |

PROTOCOL

| | |
|---|---|
| Kinase Assay ^[1] | <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 [³H]-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 [³H]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 IC₅₀ values are determined graphically from plots of percent inhibition vs inhibitor concentration^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> |
| Cell Assay ^[2] | <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% CO₂, 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% CO₂. 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^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> |
| Animal Administration ^[2] | <p>Mice^[2]</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) mm³, respectively^[2].</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 Mar 12.
- CNS Neurosci Ther. 2021 Jan 18.

- Preprints. 2021, 2021060097.
- Patent. US20180263995A1.

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REFERENCES

[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.

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

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