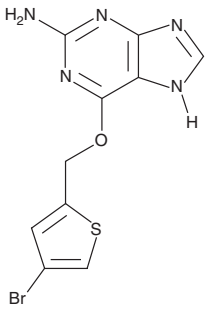
PRODUCT INFORMATION

Lomeguatrib

Item No. 11732

CAS Registry No.:	192441-08-0
Formal Name:	6-[(4-bromo-2-thienyl)methoxy]-9H-purin-2-amine
Synonym:	PaTrin 2
MF:	$C_{10}H_8BrN_5OS$
FW:	326.2
Purity:	≥98%
UV/Vis.:	λ_{max}: 239, 284 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

Lomeguatrib is supplied as a crystalline solid. A stock solution may be made by dissolving the lomeguatrib in the solvent of choice. Lomeguatrib is soluble in organic solvents such as DMSO and dimethyl formamide, which should be purged with an inert gas. The solubility of lomeguatrib in these solvents is approximately 5 and 10 mg/ml, respectively.

Lomeguatrib is sparingly soluble in aqueous solutions. To enhance aqueous solubility, dilute the organic solvent solution into aqueous buffers or isotonic saline. If performing biological experiments, ensure the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. We do not recommend storing the aqueous solution for more than one day.

Description

O^6-Methylguanine-DNA methyltransferase (MGMT) (Item No. 11176) is a DNA repair protein which removes an alkyl group from the O^6 position on guanine in an autoinactivating reaction.[1] Although important in normal DNA repair, this reaction confers resistance to treatments that use O^6-alkylating agents to produce cytotoxicity, *e.g.*, in cancer.[2,3] Lomeguatrib is a modified quanine base which acts as a pseudosubstrate inactivator of MGMT (IC_{50} = ~3 nM).[1,2] A non-toxic compound, lomeguatrib completely inactivates MGMT in human prostate and colorectal tumors when given as a single 120 mg oral dose and in primary central nervous system cancers at 160 mg.[4,5]

References

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2. Clemons, M., Kelly, J., Watson, A.J., *et al*. O^6-(4-bromothenyl)guanine reverses temozolomide resistance in human breast tumour MCF-7 cells and xenografts. *Br. J. Cancer* **93**, 1152-1156 (2005).
3. Marchesi, F., Turriziani, M., Tortorelli, G., *et al*. Triazene compounds: Mechanism of action and related DNA repair systems. *Pharmacol. Res*. **56(4)**, 275-287 (2007).
4. Ranson, M., Middleton, M.R., Bridgewater, J., *et al*. Lomeguatrib, a potent inhibitor of O^6-alkylguanine-DNA-alkyltransferase: Phase I safety, pharmacodynamic, and pharmacokinetic trial and evaluation in combination with temozolomide in patients with advanced solid tumors. *Clin. Cancer Res*. **12**, 1577-1584 (2006).
5. Watson, A.J., Sabharwal, A., Thorncroft, M., *et al*. Tumor O^6-methylguanine-DNA methyltransferase inactivation by oral lomeguatrib. *Clin. Cancer Res*. **16(2)**, 743-749 (2010).

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