

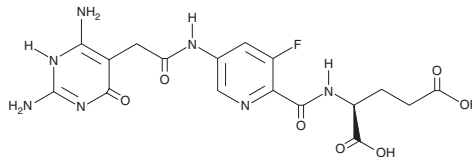
PRODUCT INFORMATION



TH9619

Item No. 45380

CAS Registry No.: 2379556-22-4
Formal Name: N-[[5-[[2-(2,4-diamino-1,6-dihydro-6-oxo-5-pyrimidinyl)acetyl]amino]-3-fluoro-2-pyridinyl]carbonyl]-L-glutamic acid
MF: C₁₇H₁₈FN₇O₇
FW: 451.4
Purity: ≥98%
Supplied as: A 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

TH9619 is supplied as a solid. A stock solution may be made by dissolving the TH9619 in the solvent of choice, which should be purged with an inert gas. TH9619 is slightly soluble (0.1-1 mg/ml) in DMSO.

Description

TH9619 is an inhibitor of methylenetetrahydrofolate dehydrogenase 1 (MTHFD1), MTHFD2, and MTHFD2L (IC₅₀s = 16, 47, and 47 nM, respectively), enzymes often overexpressed in cancer.¹ It inhibits nuclear MTHFD2 and cytoplasmic MTHFD1 but not mitochondrial MTHFD2, leading to an increase in 10-formyl-tetrahydrofolate (10-CHO-THF), thymidylate depletion, and cell death.² It is selective for MTHFD1 and MTHFD2 over a panel of 44 kinases at 12 μM and reduces proliferation in a panel of acute myeloid leukemia (AML) cells, including HL-60 and THP-1 cells, in a concentration-dependent manner. TH9619 (50 nM) impairs DNA replication in HL-60 and THP-1 cells but not non-tumorigenic LCL-534 and LCL-889 lymphocytes. It increases survival in an HL-60 mouse xenograft model when administered at a dose of 30 mg/kg twice per day in combination with a low-folate diet.

References

1. Bonagas, N., Gustafsson, N.M.S., Henriksson, M., *et al.* Pharmacological targeting of MTHFD2 suppresses acute myeloid leukemia by inducing thymidine depletion and replication stress. *Nat. Cancer* **3**(2), 156-172 (2022).
2. Green, A.C., Marttila, P., Kiweler, N., *et al.* Formate overflow drives toxic folate trapping in MTHFD1 inhibited cancer cells. *Nat. Metab.* **5**(4), 642-659 (2023).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the [complete](#) Safety Data Sheet, which has been sent via email to your institution.

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