PRODUCT INFORMATION



LY345899

Item No. 36627

CAS Registry No.: 10538-99-5

Formal Name: N-[4-(3-amino-1,2,5,6,6a,7-hexahydro-

1,9-dioxoimidazo[1,5-f]pteridin-8(9H)-yl)

benzoyl]-L-glutamic acid

MF: $C_{20}H_{21}N_7O_7$ FW: 471.4

≥98% **Purity:** UV/Vis.: λ_{max} : 293 nm

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

LY345899 is supplied as a solid. A stock solution may be made by dissolving the LY345899 in the solvent of choice, which should be purged with an inert gas. LY345899 is soluble in DMSO.

Description

LY345899 is an inhibitor of methylenetetrahydrofolate dehydrogenase 1 (MTHFD1) and MTHFD2 (IC₅₀s = 96 and 663 nM, respectively). It decreases the NADPH-to-NADP+ (NADPH/NADP+) and reduced glutathione-to-oxidized glutathione (GSH/GSSG) ratios and increases the production of reactive oxygen species (ROS) in HCT116, SW620, and LoVo colorectal cancer cells when used at a concentration of 10 μM.² LY345899 is cytotoxic to SW620 and LoVo cells, an effect that can be reversed by the antioxidant N-acetyl-L-cysteine (NAC; Item No. 20261). In vivo, LY345899 (10 mg/kg) reduces tumor growth in a patient-derived xenograft (PDX) mouse model of colorectal cancer.

References

- 1. Gustafsson, R., Jemth, A.-S., Gustafsson, N.M.S., et al. Crystal structure of the emerging cancer target MTHFD2 in complex with a substrate-based inhibitor. Cancer Res. 77(4), 937-948 (2017).
- 2. Ju, H.-Q., Lu, Y.-X., Chen, D.-L., et al. Modulation of redox homeostasis by inhibition of MTHFD2 in colorectal cancer: Mechanisms and therapeutic implications. J. Natl. Cancer Inst. 111(6), 584-596 (2109).

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

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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