PRODUCT INFORMATION

GSK199 (hydrochloride)

Item No. 17489

Formal Name: [(3R)-3-amino-1-piperidinyl][2-(1-ethyl-1H-pyrrolo[2,3-b]pyridin-2-yl)-7-methoxy-1-methyl-1H-benzimidazol-5-yl]-methanone, monohydrochloride

MF: $C_{24}H_{28}N_6O_2 \bullet HCl$

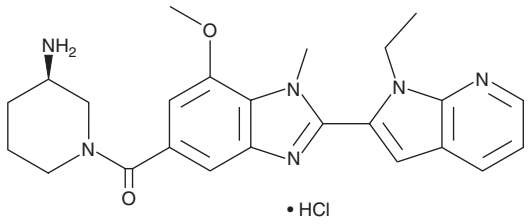
FW: 469.0

Purity: ≥98%

Stability: ≥2 years at -20°C

Supplied as: A crystalline solid

UV/Vis.: λ_{max}: 219, 244, 309 nm



Laboratory Procedures

For long term storage, we suggest that GSK199 (hydrochloride) be stored as supplied at -20°C. It should be stable for at least two years.

GSK199 (hydrochloride) is supplied as a crystalline solid. A stock solution may be made by dissolving the GSK199 (hydrochloride) in the solvent of choice. GSK199 (hydrochloride) is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of GSK199 (hydrochloride) in these solvents is approximately 30 mg/ml.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of GSK199 (hydrochloride) can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of GSK199 (hydrochloride) in PBS, pH 7.2, is approximately 10 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Description

Protein arginine deiminase 4 (PAD4) mediates the transformation of protein arginine into citrulline. Citrullination of proteins has normal roles in gene regulation and pathological roles in immunological and inflammatory diseases.[1] GSK199 is a reversible inhibitor of PAD4 (IC_{50} = 200 nM) that binds to the low-calcium form of the enzyme and is selective for PAD4 over PAD1-3.[2] It is less potent than the related PAD4 inhibitor GSK484 (Item No. 17488), which demonstrates an IC_{50} value of 50 nM.[2] GSK199 can inhibit the citrullination of PAD4 target proteins and diminish the formation of neutrophil extracellular traps in mouse neutrophils.[2]

References

1. Jones, J.E., Causey, C.P., Knuckley, B., *et al.* Protein arginine deiminase 4 (PAD4): Current understanding and future therapeutic potential. *Curr. Opin. Drug Discov. Devel.* **12(5)**, 616-627 (2009).
2. Lewis, H.D., Liddle, J., Coote, J.E., *et al.* Inhibition of PAD4 activity is sufficient to disrupt mouse and human NET formation. *Nat. Chem. Biol.* **11(3)**, 189-191 (2015).

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