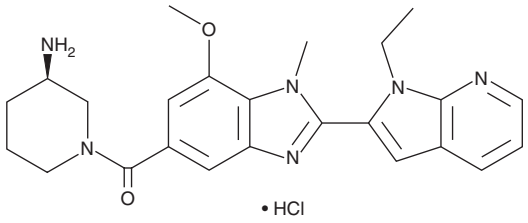
PRODUCT INFORMATION

GSK 199 (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%
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

GSK 199 (hydrochloride) is supplied as a crystalline solid. A stock solution may be made by dissolving the GSK 199 (hydrochloride) in the solvent of choice, which should be purged with an inert gas. GSK 199 (hydrochloride) is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of GSK 199 (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 GSK 199 (hydrochloride) can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of GSK 199 (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

GSK 199 is an inhibitor of peptidyl arginine deiminase 4 (PAD4; IC_{50} = 200 nM in the absence of calcium).[1] It selectively inhibits the production of citrulline by PAD4 over PAD1, PAD2, and PAD3 in kinetic assays. GSK 199 (10 µM) prevents histone H3 citrullination and neutrophil extracellular trap (NET) formation induced by ionomycin (Item No. 10004974) in isolated mouse peripheral blood neutrophils. It reduces human coronavirus OC43 (HCoV-OC43) replication in infected MRC-5 cells (IC_{50} = 0.6 µM).[2] *In vivo*, GSK 199 (10 and 30 mg/kg) reduces complement C3 deposition in the synovium and cartilage but does not reduce total synovial or serum citrulline levels in a mouse model of collagen-induced arthritis.[3] It reduces disease severity in the same model when administered at a dose of 30 mg/kg. GSK 199 (30 mg/kg) also reduces plasma NET levels and brain infarct volume, as well as improves neurological outcomes, in a mouse model of ischemic stroke induced by transient middle cerebral artery occlusion (tMCAO).[4]

References

1. 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).
2. Pasquero, S., Gugliesi, F., Griffante, G., *et al.* Novel antiviral activity of PAD inhibitors against human beta-coronaviruses HCoV-OC43 and SARS-CoV-2. *Antiviral Res.* **200**, 105278 (2022).
3. Willis, V.C., Banda, N.K., Cordova, K.N., *et al.* Protein arginine deiminase 4 inhibition is sufficient for the amelioration of collagen-induced arthritis. *Clin. Exp. Immunol.* **188(2)**, 263-274 (2017).
4. Denorme, F., Portier, I., Rustad, J.L., *et al.* Neutrophil extracellular traps regulate ischemic stroke brain injury. *J. Clin. Invest.* **132(10)**, e154225 (2022).

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