

Product Data Sheet

Product Name: AZD7986

Cat. No.: GC19052

Chemical Properties

Cas. No. 1802148-05-5

SMILES O=C([C@H]1OCCCNC1)N[C@H](C#N)CC2=CC=C(C3=CC=C(OC(N4C)=O)C4=C3)C=C2

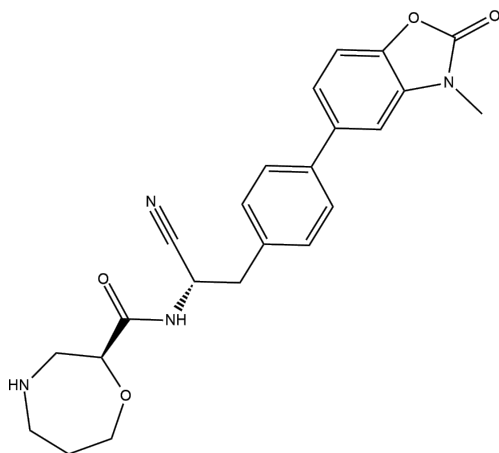
Formula $C_{23}H_{24}N_4O_4$ M.Wt 420.46

Solubility DMSO : ≥ 100 mg/mL (237.83 mM); Water : < 0.1 mg/mL (insoluble) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

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- Kinase experiment:** Activation of neutrophil serine proteases (NSPs) is assessed in vitro using primary bone marrow derived CD34+ neutrophil progenitor cells. Cells are cultured in media supplemented with rhSCF and rhIL-3 for 7 days, and then for a further 7 days in the presence of G-CSF and different concentrations of AZD7986 (38 pM to 10 μ M). After harvesting and lysis with 10% Triton X-100 buffer, cell lysates are kept at -20°C until NSP activity analysis[1].
- Cell experiment:** Cellular potency is studied using the DPP1-expressing monocytic U937 cell line. Briefly, cells grown in RPMI are plated on 384-well polypropylene v-bottom plates at a density of 5×10⁵ cells/mL per well. Added to this is 10 μ L of AZD7986 at 37°C for 60 min, followed by 350 μ M Gly-Phe-AFC. The well fluorescence is read using a multilabel plate reader. Data are analyzed to calculate pIC₅₀ values[1].
- Animal experiment:** Rats are used for the in vivo study. Naive rats are dosed orally twice daily with AZD7986 at 0.2, 2, and 20 mg/kg/day for 8 days. At termination, bone marrow is taken by femoral aspiration for neutrophil serine proteases (NSPs) activity analysis using commercial synthetic peptide substrates[1].

References:

[1]. Doyle K, et al. Discovery of Second Generation Reversible Covalent DPP1 Inhibitors Leading to an Oxazepane Amidoacetonitrile Based Clinical Candidate (AZD7986). J Med Chem. 2016 Oct 27;59(20):9457-9472.

Background

AZD7986 is a Dipeptidyl peptidase 1 (DPP1) inhibitor with pIC₅₀s of 6.85, 7.6, 7.7, 7.8, and 7.8 in human, mouse, rat, dog and rabbit, respectively.

Results from cell assay show that AZD7986 is a Dipeptidyl peptidase 1 (DPP1) inhibitor with pIC₅₀s of 6.85, 7.6, 7.7, 7.8, and 7.8 in human, mouse, rat, dog and rabbit, respectively. AZD7986 is stable

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in the propionaldehyde reactivity assay, with a half-life over 50 h. After differentiation in the presence of AZD7986 (38 pM to 10 uM), concentration-dependent decreases in cell lysate enzyme activity are observed for DPP1, as well as for all of the three NSPs, NE, Pr3, and CatG. AZD7986 inhibits activation of all three NSPs in a concentration dependent manner, with pIC₅₀ values of around 7 for all three NSPs. The reduction of the activities is almost complete, with NE, Pr3, and CatG activities reduced to 4 to 10% of control at 10 uM AZD7986[1].

AZD7986 shows good stability in plasma, with a half life of >10 h. AZD7986 inhibits activation of NE and Pr3, but not CatG, in bone marrow cell lysates in a dose dependent manner in vivo[1].

References:

[1]. Doyle K, et al. Discovery of Second Generation Reversible Covalent DPP1 Inhibitors Leading to an Oxazepane Amidoacetonitrile Based Clinical Candidate (AZD7986). J Med Chem. 2016 Oct 27;59(20):9457-9472.

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