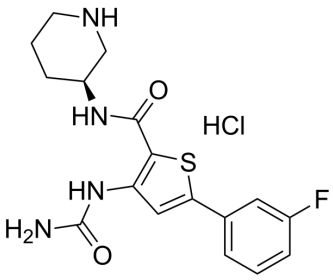
AZD-7762 hydrochloride

Cat. No.:	HY-10992A
CAS No.:	1246094-78-9
Molecular Formula:	$C_{17}H_{20}ClFN_4O_2S$
Molecular Weight:	398.88
Target:	Checkpoint Kinase (Chk)
Pathway:	Cell Cycle/DNA Damage
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	AZD-7762 hydrochloride is a potent ATP-competitive checkpoint kinase (Chk) inhibitor in with an IC_{50} of 5 nM for Chk1.	
IC_{50} & Target	Chk1 5 nM (IC_{50})	Chk2 5 nM (IC_{50})
In Vitro	AZD-7762 hydrochloride (AZD7762) is an equally potent inhibitor of Chk1 and Chk2 in vitro. AZD-7762 hydrochloride potently inhibits Chk1 and Chk2, abrogates DNA damage-induced S and G_2 checkpoints, enhances the efficacy of NSC 613327 and SKF 104864A, and modulates downstream checkpoint pathway proteins. AZD-7762 hydrochloride potently inhibits Chk1 phosphorylation of a cdc25C peptide with an IC_{50} of 5 nM as measured by a scintillation proximity assay. The K_i for AZD-7762 hydrochloride is determined to be 3.6 nM. Kinetic characterization suggests that AZD-7762 hydrochloride binds in the ATP-binding site of Chk1 and is thought to compete directly for ATP binding in a reversible manner. AZD-7762 hydrochloride is shown to abrogate the G_2 arrest induced by Camptothecin with an average EC_{50} of 10 nM (n=12) and maximal abrogation in the range of 100 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	
In Vivo	In rat H460-DNp53 xenograft studies, AZD-7762 hydrochloride (10 mg/kg and 20 mg/kg) potentiates the antitumor activity of NSC 613327 in a dose-dependent manner. That is, the inhibition rate (%T/C) decreases to 48% and 32%, respectively, with increasing dose. In a mouse xenograft study in combination with CPT-11, treatment with AZD-7762 hydrochloride in combination with CPT-11 significantly increased CPT-11 activity with a significant increase in %T/C to -66% and -67%, respectively[1]. AZD7762 hydrochloride in combination with CX-5461 induces Tp53-null ($Tp53^{-/-}$) Eμ-Myc in vitro and in vivo Lymphoma cell death[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	

CUSTOMER VALIDATION

- Nat Nanotechnol. 2021 Jul;16(7):830-839.
- Cell Metab. 2022 Feb 7;34(3):424-440.e7.
- Sci Transl Med. 2021 Jan 20;13(577):eaba7401.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.

- Acta Pharmacol Sin. 2020 Aug 27.

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REFERENCES

[1]. Zabludoff SD, et al. AZD7762, a novel checkpoint kinase inhibitor, drives checkpoint abrogation and potentiates DNA-targeted therapies. Mol Cancer Ther. 2008 Sep;7(9):2955-66.

[2]. Quin J, et al. Inhibition of RNA polymerase I transcription initiation by CX-5461 activates non-canonical ATM/ATR signaling. Oncotarget. 2016 Aug 2;7(31):49800-49818.

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