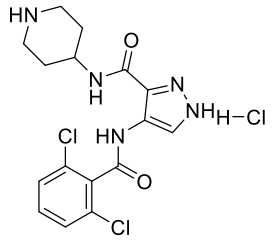
Product data sheet

MedKoo Cat#: 200320 Name: AT-7519 HCl CAS#: 902135-91-5 (HCl) Chemical Formula: $C_{16}H_{18}Cl_3N_5O_2$ Molecular Weight: 418.7	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

AT-7519 is an orally bioavailable small molecule CDK inhibitor with potential antineoplastic activity. AT7519M selectively binds to and inhibits cyclin dependent kinases (CDKs), which may result in cell cycle arrest, induction of apoptosis, and inhibition of tumor cell proliferation. CDKs are serine/theronine kinases involved in regulation of the cell cycle and may be overexpressed in some types of cancer cells.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	125.67	300.14
DMF	30.0	71.65
Ethanol	16.5	39.41
PBS (pH 7.2)	0.5	1.19
Water	43.0	102.70

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.39 mL	11.94 mL	23.88 mL
5 mM	0.48 mL	2.39 mL	4.78 mL
10 mM	0.24 mL	1.19 mL	2.39 mL
50 mM	0.05 mL	0.24 mL	0.48 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Pourbagheri-Sigaroodi A, Safaroghli-Azar A, Shanaki M, Yousefi AM, Anjam Najmedini A, Bashash D. Inhibition of Cyclin-dependent Kinase (CDK) Decreased Survival of NB4 Leukemic Cells: Proposing a p53-Independent Sensitivity of Leukemic Cells to Multi-CDKs Inhibitor AT7519. Iran J Pharm Res. 2020 Summer;19(3):144-155. doi: 10.22037/ijpr.2020.113170.14148. PMID: 33680018; PMCID: PMC7758003.

2. Zabihi M, Safaroghli-Azar A, Gharehbaghian A, Allahbakhshian Farsani M, Bashash D. CDK Blockade Using AT7519 Suppresses Acute Myeloid Leukemia Cell Survival through the Inhibition of Autophagy and Intensifies the Anti-leukemic Effect of Arsenic Trioxide. Iran J Pharm Res. 2019 Fall;18(Suppl1):119-131. doi: 10.22037/ijpr.2019.112560.13827. PMID: 32802093; PMCID: PMC7393062.

In vivo study

1. Dolman ME, Poon E, Ebus ME, den Hartog IJ, van Noesel CJ, Jamin Y, Hallsworth A, Robinson SP, Petrie K, Sparidans RW, Kok RJ, Versteeg R, Caron HN, Chesler L, Molenaar JJ. Cyclin-Dependent Kinase Inhibitor AT7519 as a Potential Drug for MYCN-

Dependent Neuroblastoma. Clin Cancer Res. 2015 Nov 15;21(22):5100-9. doi: 10.1158/1078-0432.CCR-15-0313. Epub 2015 Jul 22. PMID: 26202950; PMCID: PMC4645454.
2. Alessandri AL, Duffin R, Leitch AE, Lucas CD, Sheldrake TA, Dorward DA, Hirani N, Pinho V, de Sousa LP, Teixeira MM, Lyons JF, Haslett C, Rossi AG. Induction of eosinophil apoptosis by the cyclin-dependent kinase inhibitor AT7519 promotes the resolution of eosinophil-dominant allergic inflammation. PLoS One. 2011;6(9):e25683. doi: 10.1371/journal.pone.0025683. Epub 2011 Sep 30. PMID: 21984938; PMCID: PMC3184151.

7. Bioactivity

Biological target:

AT7519 Hydrochloride is an inhibitor of CDKs, with IC50s of 210, 47, 100, 13, 170, and <10 nM for CDK1, CDK2, CDK4 to CDK6, and CDK9, respectively.

In vitro activity

To investigate whether AT7519-induced cytotoxic effects were plausibly due to the apoptosis induction, the binding of annexin-V in combination with PI was analyzed by flow cytometry method. Intriguingly, FACS analysis of annexin-V/PI demonstrated that the inhibition of CDK increased the proportion of both early and late apoptotic cells, which was in agreement with the elevated sub-G1. As presented in Figure 4, AT7519 considerably increased annexin-V-positive NB4 cells from 10.8% in 100 nM to 35.8% in 500 nM of the inhibitor and also enhanced annexin-V/PI double-positive cell from 13.5% to 53.6% in 100 and 500 nM of the inhibitor, respectively. Taken together, these results showed that the inhibition of CDK using AT7519 halted NB4 cell progression, at least partly, through the induction of apoptotic pathway.

Reference: Iran J Pharm Res. 2020 Summer; 19(3): 144–155. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7758003/

In vivo activity

Mice were treated daily with i.p. injections of 5, 10 or 15 mg/kg AT7519 in a 5-days on, 2-days off schedule for three weeks consecutively. AT7519 inhibited the growth of AMC711T neuroblastoma xenografts in a dose-dependent manner, with even the lowest dose of 5 mg/kg providing a statistically significant reduction in tumour growth (Fig. 3A and Supplementary Fig. S5A). Treatment with either 10 or 15 mg/kg AT7519 almost completely blocked tumour growth, resulting in a significantly improved anticancer effect compared with 5 mg/kg AT7519 (Fig. 3A). More rapid tumour growth was observed after terminating treatment with AT7519 (Supplementary Fig. S5B). This study also tested AT7519 (15 mg/kg) in MYCN-amplified KCNR neuroblastoma xenografts and found a 50% reduction in tumour growth compared to saline control at day 17 after treatment initiation (Supplementary Fig. S5C).

Reference: Clin Cancer Res. 2015 Nov 15; 21(22): 5100–5109. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4645454/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.