AZD7507

Cat. No.: HY-117244

CAS No.: 1041852-85-0

Molecular Formula: $C_{23}H_{27}FN_6O_3$

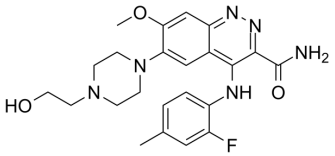
Molecular Weight: 454.5

Target: c-Fms

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 130 mg/mL (286.03 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2002 mL	11.0011 mL	22.0022 mL
	5 mM	0.4400 mL	2.2002 mL	4.4004 mL
	10 mM	0.2200 mL	1.1001 mL	2.2002 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.17 mg/mL (4.77 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.17 mg/mL (4.77 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AZD7507 is a potent and orally active CSF-1R inhibitor, with antitumor activity.

IC_{50} & Target

CSF-1R[1]

In Vitro

AZD7507 (Compound 31) inhibits the proliferation of 3T3 cells engineered to express CSF-1R and stimulated with CSF-1 (IC_{50}, 32 nM), shows inhibitory activity against hERG and NaV1.5, with IC_{50}s of >30 and 26 μM[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

AZD7507 has good rat oral PK, with in vivo clearance of 7 mL/min/kg and 42% bioavailability. In the canine L-type Ca channel assay, the IC_{50} is >20 μM[1]. AZD7507 significantly decreases the number of $CD68^+$ macrophages in mice, and also

reduces the volume and mass in mice bearing CC-LP-1 and SNU-1079 cells, but not WITT-1 cells[2].

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PROTOCOL

Animal Administration [2]

Mice[2]

Male CD1 nude mice are injected subcutaneously with 5×10^5 human ICC cells from human cell line WITT-1, CC-LP-1, or SNU-1079 (n = 24 in all cases) suspended in culture media/RGF Matrigel (Gibco) mix (1:1). Cells are engrafted bilaterally in the flank and allowed to form tumors over 3 weeks. Once palpable tumors have formed, mice are randomized into 3 groups using GraphPad online software. Xenografted mice are injected with liposomal clodronate at 4 μL/g intravenously. The control for this treatment is saline alone or liposomes not containing clodronate (both given at 4 μL/g intravenously). All of these treatments are given every 48 hours for 3 weeks. CSFR1 inhibitors AZD7507 and GW2580 are made up in sterile water containing 0.5% methylcellulose and 0.1% Tween-80. AZD7507 is given twice daily at 100 mg/kg, whereas GW2580 is given daily at 160 mg/kg. Control animals are given water containing 0.5% methylcellulose and 0.1% Tween-80. ICG-001 (5 mg/kg) or C-59 (20 mg/kg) is given by intraperitoneal injection. The vehicle for this is physiological saline. Control animals are given vehicle alone. In all cases inhibitors and vehicle are given 3 times per week[2].

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CUSTOMER VALIDATION

- Cancer Res Commun. 2023 Sep 6.

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REFERENCES

[1]. Scott DA, et al. Mitigation of cardiovascular toxicity in a series of CSF-1R inhibitors, and the identification of AZD7507. Bioorg Med Chem Lett. 2013 Aug 15;23(16):4591-6.

[2]. Boulter L, et al. WNT signaling drives cholangiocarcinoma growth and can be pharmacologically inhibited. Send to J Clin Invest. 2015 Mar 2;125(3):1269-85.

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