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产品名称：AZD8797
产品别名：AZD8797

生物活性：

Description	AZD8797 is an allosteric non-competitive and orally active modulator of the human CX3CR1 receptor; antagonizes CX3CR1 and CXCR2 with Kis of 3.9 and 2800 nM, respectively.	
IC_{50} & Target	[^{125}I]-CX3CL1-CX3CR1	^{125}I-IL-8-CXCR2
	3.9 nM (Ki, in HEK293S cells)	2800 nM (Ki, in HEK293S cells)
In Vitro	In a flow adhesion assay, AZD8797 antagonizes the natural ligand, fractalkine (CX3CL1), in both human whole blood (hWB) and in a B-lymphocyte cell line with IC_{50} values of 300 and 6 nM respectively. AZD8797 also prevents G-protein activation in a [^{35}S]GTPγS accumulation assay. AZD8797 positively modulates the CX3CL1 response at sub-micromolar concentrations in a β-arrestin recruitment assay. In equilibrium saturation binding experiments, AZD8797 reduces the maximal binding of 125I-CX3CL1 without affecting K_d[1]. AZD8797 binds selectively with high affinity to human and rat CX3CR1 (K_i of hCX3CR1, 4 nM; K_i of rCX3CR1, 7 nM, respectively). The equilibrium dissociation constant, K_B, demonstrates that AZD8797 is a very potent inhibitor for human CX3CR1 (10 nM). The potency is threefold lower for rat CX3CR1 (29 nM) and decreases even further at mouse CX3CR1 (54 nM)[2].	
In Vivo	AZD8797 treatment in Dark Agouti rats with myelin oligodendrocyte glycoprotein-induced EAE results in reduced paralysis, CNS pathology, and incidence of relapses. The compound is effective when starting treatment before onset, as well as after the acute phase[2].	

Solvent&Solubility

In Vitro:

DMSO : ≥ 150 mg/mL (371.69 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4779 mL	12.3897 mL	24.7795 mL
	5 mM	0.4956 mL	2.4779 mL	4.9559 mL
	10 mM	0.2478 mL	1.2390 mL	2.4779 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (6.19 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.19 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (6.19 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.19 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.19 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.19 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Cederblad L, et al. AZD8797 is an allosteric non-competitive modulator of the human CX3CR1 receptor. Biochem J. 2016 Mar 1;473(5):641-9. [2]. Ridderstad Wollberg A, et al. Pharmacological inhibition of the chemokine receptor CX3CR1 attenuates disease in a chronic-relapsing rat model for multiple sclerosis. Proc Natl Acad Sci U S A. 2014 Apr 8;111(14):5409-14. [3]. Sofia Karlströ, et al. Substituted 7-amino-5-thio-thiazolo[4,5-d]pyrimidines as potent and selective antagonists of the fractalkine receptor (CX3CR1). J Med Chem. 2013 Apr 25;56(8):3177-90.

实验参考：

Animal Administration	Rats: AZD8797 is formulated in 30–35% (wt/wt) hydroxy-propyl-beta-cyklodextrin and administered s.c. through osmotic minipumps. Treatment is blinded to the operator. The plasma concentration of AZD8797 is analyzed twice from each rat[2].
Kinase Assay	CHO-hCX3CR1 membranes together with different concentrations of AZD8797 are incubated in 50 mM HEPES, 100 mM NaCl, 5 mM $MgCl_2$, 10 μM GDP and 0.01% gelatin in a MicroWell 96-well plate. 0.56 μCi/mL [^{35}S]GTPγS and EC_{80} of CX3CL1 are then added. The plate is incubated at 30°C for 1 h and subsequently unbound [^{35}S]GTPγS is separated from bound by vacuum filtration to a Printed Filtermat B. The different AZD8797 concentrations are achieved by stepwise dilution in DMSO to achieve a final DMSO concentration of 1% in all wells after addition of assay buffer, regardless of AZD8797 concentration[1].
References	[1]. Cederblad L, et al. AZD8797 is an allosteric non-competitive modulator of the human CX3CR1 receptor. Biochem J. 2016 Mar 1;473(5):641-9. [2]. Ridderstad Wollberg A, et al. Pharmacological inhibition of the chemokine receptor CX3CR1 attenuates disease in a chronic-relapsing rat model for multiple sclerosis. Proc Natl Acad Sci U S A. 2014 Apr 8;111(14):5409-14. [3]. Sofia Karlströ, et al. Substituted 7-amino-5-thio-thiazolo[4,5-d]pyrimidines as potent and selective antagonists of the fractalkine receptor (CX3CR1). J Med Chem. 2013 Apr 25;56(8):3177-90.