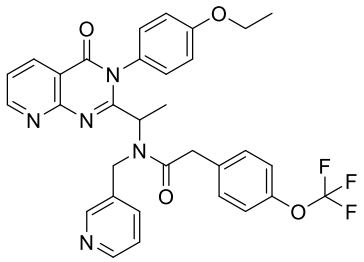
Product data sheet

MedKoo Cat#: 206468 Name: AMG-487 CAS#: 473719-41-4 Chemical Formula: $C_{32}H_{28}F_3N_5O_4$ Exact Mass: 603.20934 Molecular Weight: 603.6	
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:
AMG 487 is a potent and selective antagonist of chemokine (C-X-C motif) receptor 3 (CXCR3) with IC50 values of 8nM and 8.2nM for I-IP-10 and I-ITAC, respectively. AMG 487 prevents the chemokines I-IP-10 and I-ITAC from binding to CXCR3. In the cellular assays, AMG 487 inhibits CXCR3-mediated cell migration with IC50 values of 8nM, 15nM and 36nM for I-IP-10, I-ITAC and MIG, respectively.

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	41	67.93

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.66 mL	8.28 mL	16.57 mL
5 mM	0.33 mL	1.66 mL	3.31 mL
10 mM	0.17 mL	0.83 mL	1.66 mL
50 mM	0.03 mL	0.17 mL	0.33 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. Qin C, Liu H, Tang B, Cao M, Yu Z, Liu B, Liu W, Dong Y, Ren H. In Vitro Immunological Effects of CXCR3 Inhibitor AMG487 on Dendritic Cells. Arch Immunol Ther Exp (Warsz). 2020 Apr 1;68(2):11. doi: 10.1007/s00005-020-00577-3. PMID: 32239302.

2. Cambien B, Karimdjee BF, Richard-Fiardo P, Bziouech H, Barthel R, Millet MA, Martini V, Birnbaum D, Scoazec JY, Abello J, Al Saati T, Johnson MG, Sullivan TJ, Medina JC, Collins TL, Schmid-Alliana A, Schmid-Antomarchi H. Organ-specific inhibition of metastatic colon carcinoma by CXCR3 antagonism. Br J Cancer. 2009 Jun 2;100(11):1755-64. doi: 10.1038/sj.bjc.6605078. Epub 2009 May 12. PMID: 19436305; PMCID: PMC2695685.

In vivo study

1. Bakheet SA, Ansari MA, Nadeem A, Attia SM, Alhoshani AR, Gul G, Al-Qahtani QH, Albekairi NA, Ibrahim KE, Ahmad SF. CXCR3 antagonist AMG487 suppresses rheumatoid arthritis pathogenesis and progression by shifting the Th17/Treg cell balance. Cell Signal. 2019 Dec;64:109395. doi: 10.1016/j.cellsig.2019.109395. Epub 2019 Aug 23. PMID: 31449849.

2. Cambien B, Karimdjee BF, Richard-Fiardo P, Bziouech H, Barthel R, Millet MA, Martini V, Birnbaum D, Scoazec JY, Abello J, Al Saati T, Johnson MG, Sullivan TJ, Medina JC, Collins TL, Schmid-Alliana A, Schmid-Antomarchi H. Organ-specific inhibition of

metastatic colon carcinoma by CXCR3 antagonism. Br J Cancer. 2009 Jun 2;100(11):1755-64. doi: 10.1038/sj.bjc.6605078. Epub 2009 May 12. PMID: 19436305; PMCID: PMC2695685.

7. Bioactivity

Biological target:

AMG 487 is an orally active and selective antagonist of CXC chemokine receptor 3 (CXCR3) which inhibits the binding of CXCL10 and CXCL11 to CXCR3 with IC50s of 8.0 and 8.2 nM, respectively.

In vitro activity

The effect of AMG 487 on dendritic cell (DC) biology and function was investigated. The expression of co-stimulatory markers on DCs was reduced, indicating the semi-mature state of DC when AMG 487 was added throughout the in vitro differentiation period. Additionally, when added solely during the final lipopolysaccharide-induced activation step, AMG 487 inhibited DC activation, as demonstrated by a decreased expression of activation markers. AMG487 also promoted the expression of PD-L2 and impaired the ability to induce antigen-specific T cell responses. Our results demonstrated that AMG 487 significantly affects DC maturity in vitro and function leading to impaired T cell activation, inducing DCs to have characteristics similar to tolerogenic DCs. AMG 487 may directly play an immunomodulatory role during DC development and functional shaping.

Reference: Arch Immunol Ther Exp (Warsz). 2020 Apr 1;68(2):11. https://dx.doi.org/10.1007/s00005-020-00577-3

In vivo activity

This study investigated the role of AMG487, a selective CXCR3 antagonist, in DBA/1J mice bearing collagen-induced arthritis (CIA). Following induction of CIA, animals were treated with 5 mg/kg AMG487 intraperitoneally every 48 h, starting from day 21 until day 41 and evaluated for clinical score, and histological hallmarks of arthritic inflammation. The effect of AMG487 on Th1 (T-bet), Th17 (IL-17A, RORγt, STAT3), Th22 (IL-22), and T regulatory (Treg; Foxp3 and IL-10) cells in splenic CXCR3+ and CD4+ T cells was investigated using flow cytometry. The effect of AMG487 on T-bet, RORγt, IL-17A, IL-22, Foxp3, and IL-10 at both mRNA and protein levels was assessed using RT-PCR and Western blot analyses of knee samples. The severity of clinical scores, and histological inflammatory damage decreased significantly in AMG487-treated compared with CIA control mice. Moreover, the percentage of Th1, Th17, and Th22 cells decreased significantly and that of Treg cells increased in AMG487-treated mice. It was further observed that AMG487-treatment downregulated T-bet, IL-17A, RORγt, and IL-22, whereas it upregulated Foxp3 and IL-10 mRNA and protein levels. This study demonstrates the antiarthritic effects of AMG487 in CIA animal model and supports the development of CXCR3 antagonists as a novel strategy for the treatment of inflammatory and arthritic conditions.

Reference: Cell Signal. 2019 Dec;64:109395. https://linkinghub.elsevier.com/retrieve/pii/S0898-6568(19)30191-3