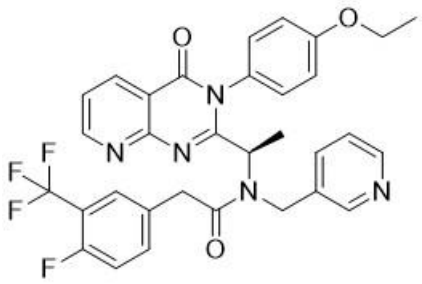
Product data sheet

MedKoo Cat#: 206469 Name: NBI-74330 CAS#: 855527-92-3 (R-isomer) Chemical Formula: $C_{32}H_{27}F_4N_5O_3$ Exact Mass: 605.205 Molecular Weight: 605.59	
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:
NBI-74330 is an antagonist of CXC chemokine receptor 3 (CXCR3) with IC50 values of 7nM to18nM. NBI-74330 attenuates atherosclerotic plaque formation in LDL receptor-deficient mice. Chemokine receptor CXCR3 promotes growth of glioma. CXCR3 antagonism exerts a direct anti-glioma effect and this receptor may be a potential therapeutic target for treating human GBM.

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	100	165.1

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.65 mL	8.26 mL	16.51 mL
5 mM	0.33 mL	1.65 mL	3.30 mL
10 mM	0.17 mL	0.83 mL	1.65 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. Piotrowska A, Rojewska E, Pawlik K, Kreiner G, Ciechanowska A, Makuch W, Zychowska M, Mika J. Pharmacological blockade of CXCR3 by (±)-NBI-74330 reduces neuropathic pain and enhances opioid effectiveness - Evidence from in vivo and in vitro studies. Biochim Biophys Acta Mol Basis Dis. 2018 Oct;1864(10):3418-3437. doi: 10.1016/j.bbadis.2018.07.032. Epub 2018 Aug 1. PMID: 30076959.
2. Liu C, Luo D, Reynolds BA, Meher G, Katritzky AR, Lu B, Gerard CJ, Bhadha CP, Harrison JK. Chemokine receptor CXCR3 promotes growth of glioma. Carcinogenesis. 2011 Feb;32(2):129-37. doi: 10.1093/carcin/bgq224. Epub 2010 Nov 3. PMID: 21051441; PMCID: PMC3026840.

In vivo study

1. Phan QT, Tan WH, Liu R, Sundaram S, Buettner A, Kneitz S, Cheong B, Vyas H, Mathavan S, Schartl M, Winkler C. Cxcl9l and Cxcr3.2 regulate recruitment of osteoclast progenitors to bone matrix in a medaka osteoporosis model. Proc Natl Acad Sci U S A. 2020 Aug 11;117(32):19276-19286. doi: 10.1073/pnas.2006093117. Epub 2020 Jul 27. PMID: 32719141; PMCID: PMC7431079.
2. Jopling LA, Watt GF, Fisher S, Birch H, Coggon S, Christie MI. Analysis of the pharmacokinetic/pharmacodynamic relationship of a small molecule CXCR3 antagonist, NBI-74330, using a murine CXCR3 internalization assay. Br J Pharmacol. 2007 Dec;152(8):1260-71. doi: 10.1038/sj.bjp.0707519. Epub 2007 Nov 5. PMID: 17982480; PMCID: PMC2190000.

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7. Bioactivity

Biological target:

NBI-74330 is a potent antagonist for CXCR3, and exhibits potent inhibition of (125I)CXCL10 and (125I)CXCL11 specific binding with Ki of 1.5 and 3.2 nM, respectively.

In vitro activity

It has been suggested that CXCR3 is important for nociception. Experiments were conducted to evaluate involvement of CXCR3 and its ligands (CXCL4, CXCL9, CXCL10, CXCL11/CCL21) in neuropathic pain. Spinal glial cells, particularly microglial, are highly activated in neuropathic pain. Additionally, the activation of these cells induces the release of a broad spectrum of nociceptive mediators including chemokines.Overall, upon these data we cannot explicitly state that CXCR3 does co-localize with microglia, however based on our in vitro study it is tempting to hypothesize that the direct influence of (±)-NBI-74330 on spinal microglia is possible, since it possesses the ability to reduce the level of CXCL10 in LPS activated microglia (Supplementary SFig. 3). In vitro studies provided evidence that (±)-NBI-74330 potently inhibits the binding of CXCL10/CXCL11 to CXCR3 in basophilic leukaemia cells , diminished CXCL11-induced chemotaxis in human T cells and block the CXCR3 internalization in murine DO11.10 cells stimulated with CXCL9, CXCL10 or CXCL11. Therefore ((±)-NBI-74330) is able to diminish the LPS-induced upregulation of CXCL10 and CXCL11 in both glial cell cultures. It is hypothesized that CXCR3 located on neuronal and – if confirmed – on part of microglial cell population, might play an important role in neuron-glial cross-talk under neuropathic pain, however this issue is just opening and interesting perspective to further studies in the future.

Biochim Biophys Acta Mol Basis Dis. 2018 Oct;1864(10):3418-3437. https://pubmed.ncbi.nlm.nih.gov/30076959/

In vivo activity

To test whether human CXCR3 inhibitors interfere with Cxcr3.2 function in medaka and block osteoclast formation, ctsk:GFP/mpeg1:mCherry/rankl:HSE:cfp transgenic medaka were treated with different doses of NBI-74330 and AMG487, two structurally related antagonists of human CXCR3, with slightly different binding affinities. The inhibitor NBI-74330 was dissolved in DMSO and 100% ethanol to make 30 mM stocks. For NBI-74330, larvae were kept in fish medium containing 30 μM NBI-74330 for 3 h prior to heat shock, changed to the pure fish medium during heat shock, and then reverted to drug solution for the course of the experiment. In NBI-74330–treated larvae at 1 dphs, the number of initially recruited macrophages was not significantly different from controls (Fig. 4 A and B); however, fewer macrophages were detectable in the region of the vertebral arches (Fig. 4E, white arrows). In contrast, at 2 dphs, when macrophage numbers increased strongly in controls, they remained at significantly lower levels in NBI-74330–treated larvae (Fig. 4B). Importantly, the total number of macrophages, including those in the AGM and tail region, was not significantly altered (Fig. 4C). Also osteoclast formation was strongly suppressed in NBI-74330–treated larvae (Fig. 4 A, D, and E). As a consequence, treatment with NBI-74330 protected bone integrity upon Rankl induction (Fig. 4E). NBI-74330–treated larvae showed a significant reduction of mineralization defects and were almost indistinguishable from Rankl-negative larvae (Fig. 4E). The data identifies a mechanism for progenitor recruitment to bone resorption sites and Cxcl9l and Cxcr3.2 as potential druggable regulators of bone homeostasis and osteoporosis.

Proc Natl Acad Sci U S A. 2020 Aug 11; 117(32): 19276–19286. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7431079/

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.