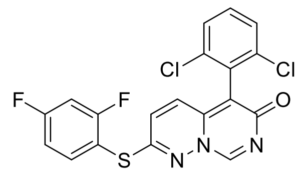
Product data sheet

MedKoo Cat#: 203163 Name: Neflamapimod CAS#: 209410-46-8 Chemical Formula: $C_{19}H_9Cl_2F_2N_3OS$ Exact Mass: 434.98114 Molecular Weight: 436.26		
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:
Neflamapimod, also known as VX-745, VRT-031745 and VD-31745, is highly potent and selective p38α inhibitor (IC50 = 10 nM). VX-745 blocks TNFα production in LPS-stimulated HWB in vitro (IC50 = 177 nM). VX-745 displays excellent enzyme activity and selectivity, has a favorable pharmacokinetic profile, and demonstrates good in vivo activity in models of inflammation.

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	40.93	93.82
DMF	30.0	68.77
DMF:PBS (pH 7.2) (1:1)	0.5	1.15
Ethanol	0.1	0.23

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.29 mL	11.46 mL	22.92 mL
5 mM	0.46 mL	2.29 mL	4.58 mL
10 mM	0.23 mL	1.15 mL	2.29 mL
50 mM	0.05 mL	0.23 mL	0.46 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. Goldsmith CS, Kim SM, Karunarathna N, Neuendorff N, Toussaint LG, Earnest DJ, Bell-Pedersen D. Inhibition of p38 MAPK activity leads to cell type-specific effects on the molecular circadian clock and time-dependent reduction of glioma cell invasiveness. BMC Cancer. 2018 Jan 10;18(1):43. doi: 10.1186/s12885-017-3896-y. Erratum in: BMC Cancer. 2019 Jan 23;19(1):101. PMID: 29316898; PMCID: PMC5761097.
2. Brown KK, Heitmeyer SA, Hookfin EB, Hsieh L, Buchalova M, Taiwo YO, Janusz MJ. P38 MAP kinase inhibitors as potential therapeutics for the treatment of joint degeneration and pain associated with osteoarthritis. J Inflamm (Lond). 2008 Dec 4;5:22. doi: 10.1186/1476-9255-5-22. PMID: 19055838; PMCID: PMC2612656.

In vivo study

1. Alam JJ, Krakovsky M, Germann U, Levy A. Continuous administration of a p38α inhibitor during the subacute phase after transient ischemia-induced stroke in the rat promotes dose-dependent functional recovery accompanied by increase in brain BDNF

protein level. PLoS One. 2020 Dec 4;15(12):e0233073. doi: 10.1371/journal.pone.0233073. PMID: 33275615; PMCID: PMC7717516.
2. Belova SP, Mochalova EP, Kostrominova TY, Shenkman BS, Nemirovskaya TL. P38α-MAPK Signaling Inhibition Attenuates Soleus Atrophy during Early Stages of Muscle Unloading. Int J Mol Sci. 2020 Apr 15;21(8):2756. doi: 10.3390/ijms21082756. PMID: 32326654; PMCID: PMC7215762.

7. Bioactivity

Biological target:

Neflamapimod (VX-745) is a blood-brain barrier penetrant and inhibitor of p38α inhibitor with an IC50 for p38α of 10 nM and for p38β of 220 nM.

In vitro activity

First, VX-745 inhibition of p38 MAPK phosphorylation was examined near the peak (hour 16) and trough (hour 4) of its activity (using two different doses: 10 µM and 20 µM) (Fig. 3). Consistent with the rhythmic time course data (Fig. 1), the levels of phospho-p38 MAPK, but not total p38 MAPK, were higher at hour 16 as compared to hour 4 (Fig. 3). However, the fold change in phospho-p38 MAPK levels was greater in *Bmal1-dLuc* fibroblasts (5X) than in *Per2^{Luc}* SCN (1.5X) cells. Treatment of *Per2^{Luc}* SCN cultures with 10 µM or 20 µM VX-745 at hour 4 or 16 had no effect on the total levels of p38 MAPK, but led to a significant reduction (>83%) in phospho-p38 MAPK levels relative to time-matched controls (Fig. 3a). In *Bmal1-dLuc* fibroblasts, 10 µM and 20 µM VX-745 also had no effect on total levels of p38 MAPK, but led to significant inhibition of p38 MAPK phosphorylation when treatment occurred at hour 16. At hour 4, phospho-p38 MAPK levels were low, and no further reduction occurred upon treatment with 10 or 20 µM VX-745 (Fig. 3b).

Reference: BMC Cancer. 2018; 18: 43. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5761097/

In vivo activity

The ELISA signal in the IL-1β assay in the unaffected left brain hemisphere were below the level for noise in the assay (i.e. below LLOQ of 20 pg/mL) in all rats in all groups. However, 9 of 18 animals in the each of the vehicle and 1.5 mg/kg neflamapimod groups and 6 of 18 animals in the 4.5 mg/kg neflamapimod group had quantifiable IL-1β levels above 20 pg/mL in the injured right brain hemisphere, indicating that despite being six weeks from acute the stroke there was still detectable residual inflammation in a substantial percentage of the animals. Quantifiable IL-1β levels ranged from 21.3 pg/mL to 203.5 pg/mL, though all but three rats had levels below 100 pg/mL (S3 Table). The mean±SD IL-1β levels in the right hemisphere was 44.3.3±55.7 pg/ml in the vehicle group, 30.8±25.9 pg/ml in the 1.5 mg/kg neflamapimod group and 28.5±32.4 pg/ml in the 4.5 mg/kg group; with no statistically significant difference between these groups.

Reference: PLoS One. 2020; 15(12): e0233073. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7717516/

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.