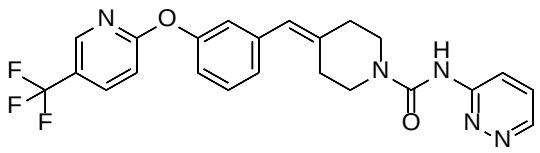
Product data sheet

MedKoo Cat#: 522480 Name: PF-04457845 CAS: 1020315-31-4 Chemical Formula: $C_{23}H_{20}F_3N_5O_2$ Exact Mass: 455.1569 Molecular Weight: 455.4412	
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:
PF-04457845 is a potent and exquisitely selective inhibitor of the enzyme fatty acid amide hydrolase (FAAH), with an IC50 of 7.2nM, and both analgesic and antiinflammatory effects in animal studies comparable to naproxen. It has been well tolerated in human trials even at high dose ranges with no evidence for cognitive dysfunction, and has completed Phase II clinical trials for the treatment of osteoarthritis, but was found to be ineffective.

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
DMF	25.0	54.89
DMF:PBS (pH 7.2) (1:5)	0.16	0.35
DMSO	64.14	140.82
Ethanol	6.04	13.25

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.20 mL	10.98 mL	21.96 mL
5 mM	0.44 mL	2.20 mL	4.39 mL
10 mM	0.22 mL	1.10 mL	2.20 mL
50 mM	0.04 mL	0.22 mL	0.44 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. Chen C, Wang W, Poklis JL, Lichtman AH, Ritter JK, Hu G, Xie D, Li N. Inactivation of fatty acid amide hydrolase protects against ischemic reperfusion injury-induced renal fibrogenesis. Biochim Biophys Acta Mol Basis Dis. 2022 Oct 1;1868(10):166456. doi: 10.1016/j.bbadis.2022.166456. Epub 2022 Jun 13. PMID: 35710061.
2. Johnson DS, Stiff C, Lazerwith SE, Kesten SR, Fay LK, Morris M, Beidler D, Liimatta MB, Smith SE, Dudley DT, Sadagopan N, Bhattachar SN, Kesten SJ, Nomanbhoy TK, Cravatt BF, Ahn K. Discovery of PF-04457845: A Highly Potent, Orally Bioavailable, and Selective Urea FAAH Inhibitor. ACS Med Chem Lett. 2011 Feb 10;2(2):91-96. doi: 10.1021/ml100190t. PMID: 21666860; PMCID: PMC3109749.

In vivo study

Product data sheet

1. Zhu M, Guo Q, Kang H, Peng R, Dong Y, Zhang Y, Wang S, Liu H, Zhao H, Dong Z, Song K, Xu S, Wang P, Chen L, Liu J, Li F. Inhibition of FAAH suppresses RANKL-induced osteoclastogenesis and attenuates ovariectomy-induced bone loss partially through repressing the IL17 pathway. FASEB J. 2023 Jan;37(1):e22690. doi: 10.1096/fj.202200911R. PMID: 36468880.
2. Ahn K, Smith SE, Liimatta MB, Beidler D, Sadagopan N, Dudley DT, Young T, Wren P, Zhang Y, Swaney S, Van Becelaere K, Blankman JL, Nomura DK, Bhattachar SN, Stiff C, Nomanbhoy TK, Weerapana E, Johnson DS, Cravatt BF. Mechanistic and pharmacological characterization of PF-04457845: a highly potent and selective fatty acid amide hydrolase inhibitor that reduces inflammatory and noninflammatory pain. J Pharmacol Exp Ther. 2011 Jul;338(1):114-24. doi: 10.1124/jpet.111.180257. Epub 2011 Apr 19. PMID: 21505060; PMCID: PMC3126636.

7. Bioactivity

Biological target:

PF-04457845 is a FAAH inhibitor with IC_{50} values is 7.2±0.63 nM and 7.4±0.62 nM for hFAAH and rFAAH.

In vitro activity

Correspondingly, a selective FAAH inhibitor, PF-04457845, inhibited the transforming growth factor-beta 1 (TGF-β1)-induced profibrogenic markers in human proximal tubular cell line (HK-2 cells) and mouse primary cultured tubular cells. Knockdown of FAAH by siRNA in HK-2 cells had similar effects as PF-04457845.

Reference: Biochim Biophys Acta Mol Basis Dis. 2022 Oct 1;1868(10):166456. https://pubmed.ncbi.nlm.nih.gov/35710061/

In vivo activity

Moreover, intragastric administration of the FAAH inhibitor PF-04457845(PF) ameliorated ovariectomy (OVX)-induced bone loss in mice. Further investigation revealed that nuclear factor κB (NF-κB) and mitogen-activated protein kinase (MAPK) pathways were inhibited by PF treatment and FAAH knockdown. RNAseq indicated that the IL17 pathway was blocked by PF, and administration of recombinant murine IL17 protein could partially restore osteoclastogenesis and activate NF-κB and MAPK pathways.

Reference: FASEB J. 2023 Jan;37(1):e22690. https://pubmed.ncbi.nlm.nih.gov/36468880/

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.