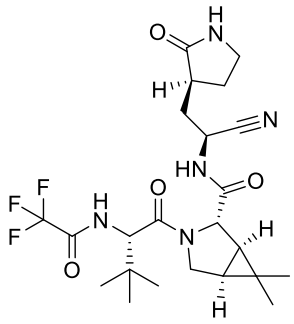
Product data sheet

MedKoo Cat#: 555985 Name: PF-07321332 CAS#: 2628280-40-8 Chemical Formula: $C_{23}H_{32}F_3N_5O_4$ Exact Mass: 499.2406 Molecular Weight: 499.5352	
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-07321332 is an orally bioavailable 3C-like protease (3CLPRO) inhibitor. This drug is being investigated for safety, tolerability, and pharmacokinetics before moving on to studies of efficacy in the treatment or prophylaxis of COVID-19. 3CLPRO is responsible for cleaving polyproteins 1a and 1ab of SARS-CoV-2. PF-07321332 is an oral COVID-19 antiviral clinical candidate. By inhibiting the main protease, PF-07321332 prevents the virus from cleaving long protein chains into the parts it needs to reproduce itself.

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	120.0	240.22

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.00 mL	10.01 mL	20.02 mL
5 mM	0.40 mL	2.00 mL	4.00 mL
10 mM	0.20 mL	1.00 mL	2.00 mL
50 mM	0.04 mL	0.20 mL	0.40 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. Pavan M, Bolcato G, Bassani D, Sturlese M, Moro S. Supervised Molecular Dynamics (SuMD) Insights into the mechanism of action of SARS-CoV-2 main protease inhibitor PF-07321332. J Enzyme Inhib Med Chem. 2021 Dec;36(1):1646-1650. doi: 10.1080/14756366.2021.1954919. PMID: 34289752.
2. Abdelnabi R, Foo CS, Jochmans D, Vangeel L, De Jonghe S, Augustijns P, Mols R, Weynand B, Wattanakul T, Hoglund RM, Tarning J, Mowbray CE, Sjö P, Escudié F, Scandale I, Chatelain E, Neyts J. The oral protease inhibitor (PF-07321332) protects Syrian hamsters against infection with SARS-CoV-2 variants of concern. Nat Commun. 2022 Feb 15;13(1):719. doi: 10.1038/s41467-022-28354-0. PMID: 35169114; PMCID: PMC8847371.

In vivo study

1. Schooley RT, Carlin AF, Beadle JR, Valiaeva N, Zhang XQ, Clark AE, McMillan RE, Leibel SL, McVicar RN, Xie J, Garretson AF, Smith VI, Murphy J, Hostetler KY. Rethinking Remdesivir: Synthesis, Antiviral Activity and Pharmacokinetics of Oral Lipid Prodrugs. Antimicrob Agents Chemother. 2021 Jul 26:AAC0115521. doi: 10.1128/AAC.01155-21. Epub ahead of print. PMID: 34310217.
2. Abdelnabi R, Foo CS, Jochmans D, Vangeel L, De Jonghe S, Augustijns P, Mols R, Weynand B, Wattanakul T, Hoglund RM, Tarning J, Mowbray CE, Sjö P, Escudié F, Scandale I, Chatelain E, Neyts J. The oral protease inhibitor (PF-07321332) protects Syrian

hamsters against infection with SARS-CoV-2 variants of concern. Nat Commun. 2022 Feb 15;13(1):719. doi: 10.1038/s41467-022-28354-0. PMID: 35169114; PMCID: PMC8847371.

7. Bioactivity

Biological target:

PF-07321332 targets the SARS-CoV-2 virus and can be used for COVID-19 reseacrch. IC50: 3CLPRO

In vitro activity

The in vitro antiviral activity of PF-332 against the four main SARS-CoV-2 VoC was first assessed in Vero E6 and A549 (overexpressing ACE2/TMPRSS2) cells, the EC50 values obtained were between 70 and 280 nM. The antiviral effect of PF-332 was next assessed in primary human airway epithelial cell (HAEC) [that had been fully differentiated into an air-liquid (ALI) culture system] that were infected with the alpha variant (B.1.1.7). When added to the culture medium at the basolateral site of the ALI's 1 h before infection (at the topical site) PF-332 (at 1 μM) completely inhibited viral replication for the entire duration of the experiment. At a concentration of 0.1 μM the inhibition was transient.

Reference: Nat Commun. 2022 Feb 15;13(1):719. https://pubmed.ncbi.nlm.nih.gov/35169114/

In vivo activity

Female hamsters (6–8 weeks) were intranasally infected with the SARS-CoV2 beta variant (lineage B.1.351) and were orally treated with PF-332 [either at 125 or 250 mg/kg/dose, twice daily (BID)] or the vehicle (i.e., the control group) for four consecutive days whereby treatment was initiated immediately before infection. Treatment resulted in a dose-dependent reduction of viral RNA copies in lung tissue; i.e., 1.1 log10 ($P = 0.0007$) and 5.8 log10 ($P < 0.0001$) reduction in, respectively, the 125 and 250 mg/kg, BID treatment groups. Likewise the 125 mg/kg BID dose resulted in a 0.7 log10 ($P = 0.03$) reduction in lung infectious virus titers and treatment with 250 mg/kg BID resulted in undetectable infectious virus levels in the lungs in all the treated animals (4.4 log10 reduction, $P < 0.0001$). No clinical signs of adverse effects were observed in any of the PF-332-treated groups. Treatment also markedly improved virus-induced lung pathology, in particular in the 250 mg/kg BID dose whereby the lung pathology score was (in 11 out of 12 animals) comparable to the baseline score of untreated, non-infected hamsters ($P < 0.0001$).

Reference: Nat Commun. 2022 Feb 15;13(1):719. https://pubmed.ncbi.nlm.nih.gov/35169114/