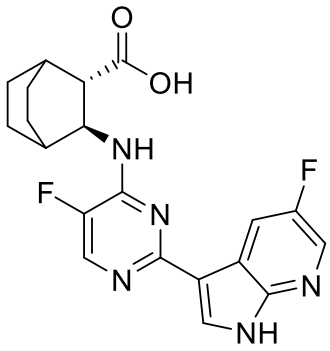
Product data sheet

MedKoo Cat#: 522612 Name: VX-787 CAS#: 1629869-44-8 (free base) Chemical Formula: $C_{20}H_{19}F_2N_5O_2$ Exact Mass: 399.1507 Molecular Weight: 399.4018	
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:
Pimodivir, also known as VX-787, JNJ-872, is a novel inhibitor of influenza virus replication that blocks the PB2 cap-snatching activity of the influenza viral polymerase complex. VX-787 binds the cap-binding domain of the PB2 subunit with a KD (dissociation constant) of 24 nM as determined by isothermal titration calorimetry (ITC). The cell-based EC50 (the concentration of compound that ensures 50% cell viability of an uninfected control) for VX-787 is 1.6 nM in a cytopathic effect (CPE) assay, with a similar EC50 in a viral RNA replication assay. VX-787 is active against a diverse panel of influenza A virus strains, including H1N1pdm09 and H5N1 strains, as well as strains with reduced susceptibility to neuraminidase inhibitors (NAIs).

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	250.38

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.50 mL	12.52 mL	25.04 mL
5 mM	0.50 mL	2.50 mL	5.01 mL
10 mM	0.25 mL	1.25 mL	2.50 mL
50 mM	0.05 mL	0.25 mL	0.50 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. Fu Y, Gaelings L, Söderholm S, Belanov S, Nandania J, Nyman TA, Matikainen S, Anders S, Velagapudi V, Kainov DE. JNJ872 inhibits influenza A virus replication without altering cellular antiviral responses. Antiviral Res. 2016 Sep;133:23-31. doi: 10.1016/j.antiviral.2016.07.008. Epub 2016 Jul 20. PMID: 27451344.

2. Byrn RA, Jones SM, Bennett HB, Bral C, Clark MP, Jacobs MD, Kwong AD, Ledeboer MW, Leeman JR, McNeil CF, Murcko MA, Nezami A, Perola E, Rijnbrand R, Saxena K, Tsai AW, Zhou Y, Charifson PS. Preclinical activity of VX-787, a first-in-class, orally bioavailable inhibitor of the influenza virus polymerase PB2 subunit. Antimicrob Agents Chemother. 2015 Mar;59(3):1569-82. doi: 10.1128/AAC.04623-14. Epub 2014 Dec 29. PMID: 25547360; PMCID: PMC4325764.

In vivo study

1. Byrn RA, Jones SM, Bennett HB, Bral C, Clark MP, Jacobs MD, Kwong AD, Ledeboer MW, Leeman JR, McNeil CF, Murcko MA, Nezami A, Perola E, Rijnbrand R, Saxena K, Tsai AW, Zhou Y, Charifson PS. Preclinical activity of VX-787, a first-in-class,

orally bioavailable inhibitor of the influenza virus polymerase PB2 subunit. Antimicrob Agents Chemother. 2015 Mar;59(3):1569-82. doi: 10.1128/AAC.04623-14. Epub 2014 Dec 29. PMID: 25547360; PMCID: PMC4325764.

2. Smee DF, Barnard DL, Jones SM. Activities of JNJ63623872 and oseltamivir against influenza A H1N1pdm and H3N2 virus infections in mice. Antiviral Res. 2016 Dec;136:45-50. doi: 10.1016/j.antiviral.2016.10.009. Epub 2016 Oct 19. PMID: 27771390.

7. Bioactivity

Biological target: Pimodivir (VX-787) is an orally bioavailable inhibitor of influenza A virus polymerases through interaction with the viral PB2 subunit.

In vitro activity

Pimodivir (VX-787) rescues macrophages from virus-mediated death at non-cytotoxic concentrations 24 hpi. The EC_{50} value for Pimodivir are 8 and 12 nM for A(H1N1) and A(H3N2) strains, respectively, whereas the CC_{50} values are >1 μM, giving selectivity indexes (SI) > 125 and > 83 for A(H1N1) and A(H3N2) strains, respectively. Pimodivir significantly attenuates the transcription of viral M1 RNA in macrophages, which are infected with A(H1N1) or A(H3N2) strains for 8 h. Pimodivir inhibits the transcription of viral but not cellular genes. Pimodivir allows some activation of IAV-mediated expression of several cellular genes, which are involved in tryptophan and nucleotide metabolism. Pimodivir possesses excellent anti-IAV but not immuno/metabolo-modulating effect.

Reference: Antiviral Res. 2016 Sep;133:23-31. https://www.sciencedirect.com/science/article/pii/S0166354216302583?via%3Dihub

In vivo activity

VX-787 shows consistent activity against the H1N1pdm09 strain and a highly pathogenic avian influenza virus A/Viet Nam/1203/2004 strain. PB2 has been reported to play a significant role in host restriction (57, 58), with a K627E substitution observed in avian strains relative to human-derived strains. VX-787 is equally effective against strains containing this K627E variant, which is outside the PB2 cap-binding site (data not shown). Targeting PB2 instead of neuraminidase in the influenza virus replication cycle provides several unique opportunities. At any point during the course of disease in vivo, there are both infected cells that need to be controlled and as-yet-uninfected cells that need to be protected; VX-787 has the potential to perform both functions. The means by which VX-787 blocks CPE in infected cells could simply be inhibition of (+)-strand viral RNA synthesis, but it is possible that other mechanisms, such as interference with influenza virus-induced host cell shutoff, are involved (59, 60). Many details of the function of PB2 remain to be elucidated. The effect of VX-787 on lung viral loads in mice is positive. At several different doses, VX-787 showed a 1 to >5 log viral load reduction relative to vehicle controls. Administration of VX-787 provides a rapid reduction in the amount of influenza A virus in the lungs of infected mice and suggests a direct effect on viral replication. This result is consistent with the observed MOI independence of VX-787; initially infected lung cells may create a local high-MOI environment that would remain under antiviral suppression by VX-787 but not be suppressed by oseltamivir. The results from this series of studies represent the first evidence that a pharmacologic inhibitor of influenza A virus PB2 effectively inhibits viral replication in vivo and successfully abrogates or attenuates influenza virus infection in mouse models of the disease.

Reference: Antimicrob Agents Chemother. 2015 Mar;59(3):1569-82. https://aac.asm.org/content/59/3/1569

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.