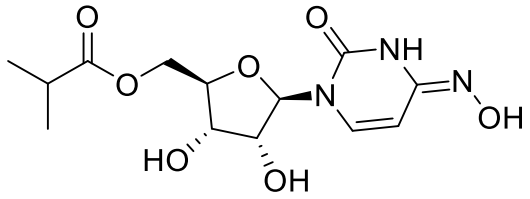
Product data sheet

MedKoo Cat#: 555745 Name: EIDD-2801 CAS#: 2349386-89-4 Chemical Formula: $C_{13}H_{19}N_3O_7$ Exact Mass: 329.1223 Molecular Weight: 329.31	
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:

Molnupiravir, also known as EIDD-2801 and MK-4482, is an orally bioavailable form of a highly potent ribonucleoside analog that inhibits the replication of multiple RNA viruses including SARS-CoV-2, the causative agent of COVID-19. EIDD-2801 has been shown to improve pulmonary function, decrease body weight loss and reduce the amount of virus in the lung. In addition to activity against coronaviruses, EIDD-2801, in laboratory studies, has demonstrated activity against seasonal and bird influenza, respiratory syncytial virus, chikungunya virus, Ebola virus, Venezuelan equine encephalitis virus, and Eastern equine encephalitis virus. EIDD-2801 is a prodrug of EIDD-1931.

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	100.0	303.67
DMF	50.0	151.83

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.04 mL	15.18 mL	30.37 mL
5 mM	0.61 mL	3.04 mL	6.07 mL
10 mM	0.30 mL	1.52 mL	3.04 mL
50 mM	0.06 mL	0.30 mL	0.61 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. Gordon CJ, Tchesnokov EP, Schinazi RF, Götte M. Molnupiravir promotes SARS-CoV-2 mutagenesis via the RNA template. J Biol Chem. 2021 May 11;297(1):100770. doi: 10.1016/j.jbc.2021.100770. Epub ahead of print. PMID: 33989635; PMCID: PMC8110631.
2. Rosenke K, Hansen F, Schwarz B, Feldmann F, Haddock E, Rosenke R, Barbian K, Meade-White K, Okumura A, Leventhal S, Hawman DW, Ricotta E, Bosio CM, Martens C, Saturday G, Feldmann H, Jarvis MA. Orally delivered MK-4482 inhibits SARS-CoV-2 replication in the Syrian hamster model. Nat Commun. 2021 Apr 16;12(1):2295. doi: 10.1038/s41467-021-22580-8. PMID: 33863887; PMCID: PMC8052374.

In vivo study

1. Rosenke K, Hansen F, Schwarz B, Feldmann F, Haddock E, Rosenke R, Barbian K, Meade-White K, Okumura A, Leventhal S, Hawman DW, Ricotta E, Bosio CM, Martens C, Saturday G, Feldmann H, Jarvis MA. Orally delivered MK-4482 inhibits SARS-

CoV-2 replication in the Syrian hamster model. Nat Commun. 2021 Apr 16;12(1):2295. doi: 10.1038/s41467-021-22580-8. PMID: 33863887; PMCID: PMC8052374.
2. Cox RM, Wolf JD, Plemper RK. Therapeutic MK-4482/EIDD-2801 Blocks SARS-CoV-2 Transmission in Ferrets. Res Sq [Preprint]. 2020 Oct 12:rs.3.rs-89433. doi: 10.21203/rs.3.rs-89433/v1. Update in: Nat Microbiol. 2020 Dec 3;: PMID: 33052328; PMCID: PMC7553152.

7. Bioactivity

Biological target:

Molnupiravir (EIDD-2801) is a bioavailable prodrug of the ribonucleoside analog EIDD-1931 that has broad spectrum antiviral activity against influenza virus and multiple coronaviruses, such as SARS-CoV-2, MERS-CoV, SARS-CoV.

In vitro activity

Molnupiravir is a broad-spectrum antiviral that is an orally bioavailable prodrug of the nucleoside analogue β-D-N4-hydroxycytidine (NHC). Molnupiravir or NHC can increase G to A and C to U transition mutations in replicating coronaviruses. These increases in mutation frequencies can be linked to increases in antiviral effects. Here, the effects of the active compound NHC 5'-triphosphate (NHC-TP) against the purified severe acute respiratory syndrome coronavirus 2 RNA-dependent RNA polymerase complex were studied. The efficiency of incorporation of natural nucleotides over the efficiency of incorporation of NHC-TP into model RNA substrates followed the order GTP (12,841) > ATP (424) > UTP (171) > CTP (30), indicating that NHC-TP competes predominantly with CTP for incorporation. No significant inhibition of RNA synthesis was noted as a result of the incorporated monophosphate in the RNA primer strand. When embedded in the template strand, NHC-monophosphate supported the formation of both NHC:G and NHC:A base pairs with similar efficiencies. The extension of the NHC:G product was modestly inhibited, but higher nucleotide concentrations could overcome this blockage. In contrast, the NHC:A base pair led to the observed G to A (G:NHC:A) or C to U (C:G:NHC:A:U) mutations. Together, these biochemical data support a mechanism of action of molnupiravir that is primarily based on RNA mutagenesis mediated via the template strand.

Reference: J Biol Chem. 2021 Jul; 297(1): 100770. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8110631/

In vivo activity

The efficacy of the MK-4482 prodrug was next assessed in the Syrian hamster model, which is regarded as a preclinical model of mild disease, with animals having self-limiting pneumonia.. Given the possibility for oral dosing, the utility of MK-4482 as a treatment following high-risk exposure was inspected. Two groups of hamsters (n = 6 per group) were treated with MK-4482 (250 mg/kg) by oral gavage 12 h and 2 h before (pre-infection treatment group) or 12 h post-infection (post-infection treatment group). Lung tissue samples were collected at the peak of virus replication and disease, day 4 post-infection, for analysis. In contrast to levels of shedding, a 1-log decrease in viral RNA was detected in the lungs of pre-infection and post-infection groups, respectively, when compared to the vehicle control group (Fig. 2d). This corresponded to a 2-log decrease in infectious virus in the lungs of the MK-4482 treated groups when compared to the vehicle controls (Fig. 2e). MK-4482 was not detected in the tissue. Then compared to the vehicle, viral genomes from MK-4482 treated animals had a significant accumulation of nucleotide substitutions (Supplementary Table 2). Together, these results are consistent with the RNA mutagenesis function of MK-4482 in the reduction of infectious virus and disease in treated animals. If adequately priced for widespread global use, MK-4482 should be considered as an oral post-exposure application for SARS-CoV-2.

Reference: Nat Commun. 2021; 12: 2295. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8052374/