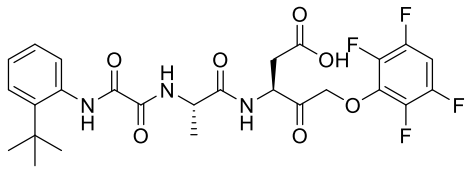
Product data sheet

MedKoo Cat#: 510230 Name: Emricasan CAS#: 254750-02-2 Chemical Formula: $C_{26}H_{27}F_4N_3O_7$ Exact Mass: 569.17851 Molecular Weight: 569.51	
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:
Emricasan, also known as IDN 6556 and PF 03491390, is a first-in-class caspase inhibitor in clinical trials for the treatment of liver diseases. Emricasan (IDN-6556) decreases liver injury and fibrosis in a murine model of non-alcoholic steatohepatitis. IDN6556 facilitates marginal mass islet engraftment in a porcine islet autotransplant model. Oral IDN-6556 may lower aminotransferase activity in patients with chronic hepatitis C. Orally-administered PF-03491390 is retained in the liver for prolonged periods with low systemic exposure, exerting a hepatoprotective effect against alpha-fas-induced liver injury in a mouse model.

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	42	73.75
Ethanol	100	175.59

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.7559 mL	8.7796 mL	17.5593 mL
5 mM	0.3512 mL	1.7559 mL	3.5119 mL
10 mM	0.1756 mL	0.8780 mL	1.7559 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. Gracia-Sancho J, Manicardi N, Ortega-Ribera M, Maeso-Díaz R, Guixé-Muntet S, Fernández-Iglesias A, Hide D, García-Calderó H, Boyer-Díaz Z, Contreras PC, Spada A, Bosch J. Emricasan Ameliorates Portal Hypertension and Liver Fibrosis in Cirrhotic Rats Through a Hepatocyte-Mediated Paracrine Mechanism. Hepatol Commun. 2019 Apr 22;3(7):987-1000. doi: 10.1002/hep4.1360. PMID: 31304452; PMCID: PMC6601324.

2. Xu M, Lee EM, Wen Z, Cheng Y, Huang WK, Qian X, Tcw J, Kouznetsova J, Ogden SC, Hammack C, Jacob F, Nguyen HN, Itkin M, Hanna C, Shinn P, Allen C, Michael SG, Simeonov A, Huang W, Christian KM, Goate A, Brennand KJ, Huang R, Xia M, Ming GL, Zheng W, Song H, Tang H. Identification of small-molecule inhibitors of Zika virus infection and induced neural cell death via a drug repurposing screen. Nat Med. 2016 Oct;22(10):1101-1107. doi: 10.1038/nm.4184. Epub 2016 Aug 29. PMID: 27571349; PMCID: PMC5386783.

In vivo study

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1. Barreyro FJ, Holod S, Finocchietto PV, Camino AM, Aquino JB, Avagnina A, Carreras MC, Poderoso JJ, Gores GJ. The pan-caspase inhibitor Emricasan (IDN-6556) decreases liver injury and fibrosis in a murine model of non-alcoholic steatohepatitis. Liver Int. 2015 Mar;35(3):953-66. doi: 10.1111/liv.12570. Epub 2014 Jun 6. PMID: 24750664.

2. Hoglen NC, Chen LS, Fisher CD, Hirakawa BP, Groessl T, Contreras PC. Characterization of IDN-6556 (3-[2-(2-tert-butyl-phenylaminooxalyl)-amino]-propionylamino]-4-oxo-5-(2,3,5,6-tetrafluoro-phenoxy)-pentanoic acid): a liver-targeted caspase inhibitor. J Pharmacol Exp Ther. 2004 May;309(2):634-40. doi: 10.1124/jpet.103.062034. Epub 2004 Jan 23. PMID: 14742742.

7. Bioactivity

Biological target: Emricasan (PF 03491390) is an orally active and irreversible pan-caspase inhibitor.

In vitro activity

Figure 7 shows that human cirrhotic hepatocytes cultured in vitro and treated with emricasan exhibit a marked amelioration in their phenotype when compared with vehicle - treated cells, with improved expression of HNF4α, abcc3 and slc22a1, and higher albumin and urea synthesis, without signs of hepatotoxicity. The number of hepatocytes at the end of the experiment were not different between groups, as indicated by the amount of RNA obtained in each experimental condition. Interestingly, the beneficial effects of the drug were not observed in hepatocytes undergoing spontaneous de - differentiation due to culture in conventional methods (data not shown).

References: Hepatol Commun. 2019 Jul; 3(7): 987–1000. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6601324/

In vivo activity

Mice fed a HFD diet demonstrate a five-fold increase in hepatocyte apoptosis by the TUNEL assay and a 1.5-fold and 1.3-fold increase in caspase-3 and-8 activities respectively; this increase in apoptosis was substantially attenuated in mice fed a HFD treated with Emricasan (HFD-Em). Likewise, liver injury and inflammation were reduced in mice fed HFD-Em as compare to HFD by measuring serum aspartate aminotransferase and alanine aminotransferase levels, NAS histological score and IL 1-β, TNF-α, monocyte chemoattractant protein (MCP-1) and C-X-C chemokine ligand-2 (CXCL2) quantitative reverse-transcription polymerase chain reaction (qPCR). These differences could not be attributed to differences in hepatic steatosis as liver triglycerides content were similar in both HFD groups. Hepatic fibrosis was reduced by Emricasan in HFD animals by decreasing αSMA (a marker for hepatic stellate cell activation), fibrosis score, Sirius red staining, hydroxyproline liver content and profibrogenic cytokines by qPCR.

Reference: Liver Int. 2015 Mar;35(3):953-66. https://onlinelibrary.wiley.com/doi/abs/10.1111/liv.12570

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.