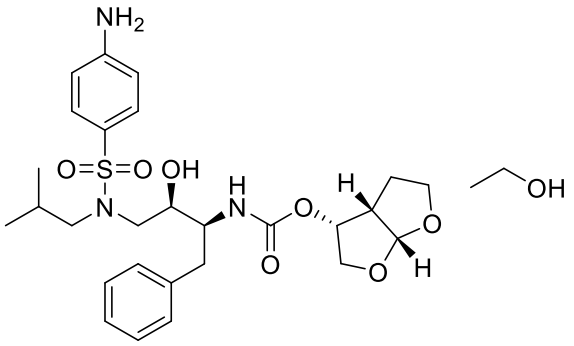
Product data sheet

MedKoo Cat#: 574651 Name: Darunavir ethanolate CAS#: 635728-49-3 (ethanolate) Chemical Formula: $C_{29}H_{43}N_3O_8S$ Exact Mass: 593.2771 Molecular Weight: 593.74	
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:
Darunavir ethanolate is an inhibitor active against HIV-1 clinical isolates with minimal cytotoxicity.

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	75.0	126.32

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.68 mL	8.42 mL	16.84 mL
5 mM	0.34 mL	1.68 mL	3.37 mL
10 mM	0.17 mL	0.84 mL	1.68 mL
50 mM	0.03 mL	0.17 mL	0.34 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. Gao X, Rosales A, Karttunen H, Bommana GM, Tandoh B, Yi Z, Habib Z, D'Agati V, Zhang W, Ross MJ. The HIV protease inhibitor darunavir prevents kidney injury via HIV-independent mechanisms. Sci Rep. 2019 Nov 1;9(1):15857. doi: 10.1038/s41598-019-52278-3. Erratum in: Sci Rep. 2020 Mar 4;10(1):4345. PMID: 31676833; PMCID: PMC6825220.

In vivo study

1. Gao X, Rosales A, Karttunen H, Bommana GM, Tandoh B, Yi Z, Habib Z, D'Agati V, Zhang W, Ross MJ. The HIV protease inhibitor darunavir prevents kidney injury via HIV-independent mechanisms. Sci Rep. 2019 Nov 1;9(1):15857. doi: 10.1038/s41598-019-52278-3. Erratum in: Sci Rep. 2020 Mar 4;10(1):4345. PMID: 31676833; PMCID: PMC6825220.

7. Bioactivity
Biological target:

Darunavir ethanolate (TMC114 Ethanolate) is a potent HIV protease inhibitor used to treat and prevent HIV/AIDS. Darunavir has a Ki of 1 nM for wild type HIV-1 protease.

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In vitro activity

To test whether DRV (Darunavir) can protect kidney cells from the deleterious effects of HIV via HIV protease-independent mechanisms, the effects of DRV on renal tubular epithelial cells (RTEC) were studied. Conditionally immortalized human RTEC (HPT1b cells) were transduced with lentiviral vectors encoding either gag/pol-deleted HIV (based on the same provirus used in Tg26 HIVAN model, which lacks HIV protease), Vpr, or control lentivirus expressing EGFP and subsequently treated with DRV or vehicle control. HIV and Vpr-transduction of HPT1b cells increased phosphorylation of Stat3 ($p < 0.01$), Src ($p < 0.01$), and Erk ($p < 0.01$) compared to cells transduced with EGFP control lentivirus and DRV significantly prevented HIV and Vpr-induced phosphorylation of Stat3 ($p < 0.01$), Src ($p < 0.01$), and Erk ($p < 0.01$) (Fig. 1A,B). Since HIV-induced expression of proinflammatory mediators, including IL-6 and IL-8 are critical mediators of HIVAN pathogenesis35, we analyzed IL-6 and IL-8 expression in control, HIV- and Vpr-transfected HPT1b cells treated with or without DRV (Fig. 1C). HIV and Vpr transduction increased the expression of IL-6 ($p < 0.01$ and $p = 0.03$ respectively) and IL-8 ($p < 0.01$) in HPT1b cells compared to control-transduced cells. HIV and Vpr-induced upregulation of IL-6 and IL-8 was abrogated by DRV (Fig. 1C, $p < 0.01$).

Reference: Sci Rep. 2019; 9: 15857. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6825220/

In vivo activity

It was next studied whether DRV can protect HIV-transgenic mice from developing the HIVAN phenotype. Four-month-old heterozygous Tg26-FVB mice were assigned to 4 treatment groups and were treated daily by oral gavage for 5 weeks with DRV, AZT, DRV + AZT, or vehicle control. Control-treated Tg26 mice developed typical histopathologic findings of HIVAN, whereas glomerulosclerosis and tubulointerstitial injury were improved in Tg26 treated with DRV. Quantitative histomorphometry demonstrated that DRV and DRV + AZT groups had significantly reduced glomerulosclerosis (Fig. 2B, $p = 0.015$, and $p = 0.029$, respectively), tubular cast formation (Fig. 2C, $p = 0.023$ and $p = 0.048$, respectively), interstitial fibrosis and tubular atrophy (Fig. 2D, $p = 0.025$ and $p = 0.017$, respectively), and interstitial inflammation (Fig. 2E, $p = 0.012$ and $p = 0.013$, respectively) compared to vehicle-treated mice. kidneys from Tg26 mice treated with vehicle control (Fig. 5A) or AZT had markedly increased levels of p-Stat3, whereas levels were similar to wild-type in DRV or DRV + AZT treated Tg26 mice. Similarly, p-Src and p-Erk were increased in kidneys of Tg26 mice treated with vehicle control or AZT, but not in those treated with DRV or DRV + AZT (Fig. 5A).

Reference: Sci Rep. 2019; 9: 15857. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6825220/