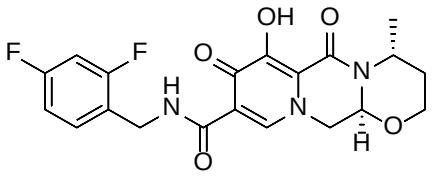
Product data sheet

MedKoo Cat#: 315142 Name: Dolutegravir CAS#: 1051375-16-6 (free) Chemical Formula: $C_{20}H_{19}F_2N_3O_5$ Exact Mass: 419.1293 Molecular Weight: 419.38	
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:
Dolutegravir, also known as GSK1349572, is a potent inhibitor of HIV integrase with an IC50 value of 2.7 nM for HIV-1 integrase-catalyzed strand transfer in vitro.1 It inhibits HIV-1 viral replication (EC50 = 0.51 nM) in peripheral blood mononuclear cells (PBMCs). Dolutegravir (DTG) is an antiretroviral medication used, together with other medication, to treat HIV/AIDS. It may also be used, as part of post exposure prophylaxis, to prevent HIV infection following potential exposure.

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	31.83	75.90
DMF	5.0	11.92
DMF:PBS (pH 7.2) (1:4)	0.20	0.48

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.38 mL	11.92 mL	23.84 mL
5 mM	0.48 mL	2.38 mL	4.77 mL
10 mM	0.24 mL	1.19 mL	2.38 mL
50 mM	0.05 mL	0.24 mL	0.48 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. Smith RA, Raugi DN, Pan C, Sow PS, Seydi M, Mullins JI, Gottlieb GS; University of Washington-Dakar HIV-2 Study Group. In vitro activity of dolutegravir against wild-type and integrase inhibitor-resistant HIV-2. Retrovirology. 2015 Feb 5;12:10. doi: 10.1186/s12977-015-0146-8. PMID: 25808007; PMCID: PMC4328052.

In vivo study

1. Heredia A, Hassounah S, Medina-Moreno S, Zapata JC, Le NM, Han Y, Foulke JS Jr, Davis C, Bryant J, Redfield RR, Wainberg MA. Monotherapy with either dolutegravir or raltegravir fails to durably suppress HIV viraemia in humanized mice. J Antimicrob Chemother. 2017 Sep 1;72(9):2570-2573. doi: 10.1093/jac/dkx195. PMID: 28637235; PMCID: PMC5890682.

7. Bioactivity
Biological target: Dolutegravir is a potent inhibitor of HIV integrase with an IC50 of 2.7 nM for HIV-1 integrase-catalyzed strand transfer.

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In vitro activity

To evaluate the potential role of dolutegravir in HIV-2 treatment, the susceptibilities of wild-type and INSTI-resistant HIV-1 and HIV-2 strains to dolutegravir were compared using single-cycle assays, spreading infections of immortalized T cells, and site-directed mutagenesis. HIV-2 group A, HIV-2 group B, and HIV-1 isolates from INSTI-naïve individuals were comparably sensitive to dolutegravir in the single-cycle assay (mean EC50 values = 1.9, 2.6, and 1.3 nM, respectively). Integrase substitutions E92Q, Y143C, E92Q + Y143C, and Q148R conferred relatively low levels of resistance to dolutegravir in HIV-2ROD9 (2- to 6-fold), but Q148K, E92Q + N155H, T97A + N155H and G140S + Q148R resulted in moderate resistance (10- to 46-fold), and the combination of T97A + Y143C in HIV-2ROD9 conferred high-level resistance (>5000-fold). In contrast, HIV-1NL4-3 mutants E92Q + N155H, G140S + Q148R, and T97A + Y143C showed 2-fold, 4-fold, and no increase in EC50, respectively, relative to the parental strain. The resistance phenotypes for E92Q + N155H, and G140S + Q148R HIV-2ROD9 were also confirmed in spreading infections of CEM-ss cells.

Reference: Retrovirology. 2015 Feb 5;12:10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4328052/

In vivo activity

The efficacy of 20 week monotherapy with dolutegravir was evaluated in humanized mice (HSC-NSG) infected with HIVBaL. Drug-untreated control mice maintained constant viraemia throughout the study. Virus isolates from these mice were susceptible to dolutegravir (EC50 of <1 nM). Mice treated with dolutegravir had plasma drug levels comparable to those in humans. Monotherapy with dolutegravir suppressed viraemia in 5/5 of mice, but viraemia rebounded in one animal. The virus from this mouse had mutations E138K, G140S, Q148H, N155H and S230R, was highly resistant to both raltegravir (EC50 of >1000 nM) and dolutegravir (EC50 of 550 nM), and replicated to levels similar to those of control viruses in PBMCs. These results suggest that monotherapy with dolutegravir does not consistently maintain HIV suppression and that dual therapy may be required in simplification strategies.

Reference: J Antimicrob Chemother. 2017 Sep 1;72(9):2570-2573. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5890682/

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.