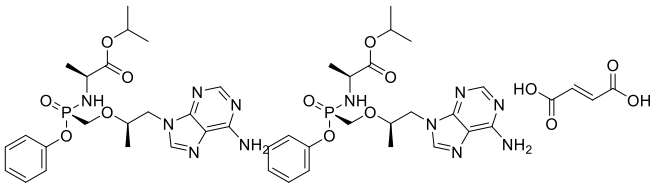
Product data sheet

MedKoo Cat#: 319909 Name: Tenofovir alafenamide hemifumarate CAS#: 1392275-56-7 (hemifumarate) Chemical Formula: $C_{46}H_{62}N_{12}O_{14}P_2$ Molecular Weight: 1069.0195	
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:

Tenofovir alafenamide hemifumarate, also known as Tenofovir alafenamide fumarate (2:1), is a nucleotide reverse transcriptase inhibitor (NRTIs) and a novel prodrug of tenofovir. By blocking reverse transcriptase, TAF prevent HIV from multiplying and can reduce the amount of HIV in the body. Tenofovir alafenamide is a prodrug, which means that it is an inactive drug. In the body, tenofovir alafenamide is converted to tenofovir diphosphate (TFV-DP). Tenofovir alafenamide fumarate was approved in November 2015 for treatment of HIV-1.

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	70.16

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	0.94 mL	4.68 mL	9.35 mL
5 mM	0.19 mL	0.94 mL	1.87 mL
10 mM	0.09 mL	0.47 mL	0.94 mL
50 mM	0.02 mL	0.09 mL	0.19 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. Su JT, Simpson SM, Sung S, Tfaily EB, Veazey R, Marzinke M, Qiu J, Watrous D, Widanapathirana L, Pearson E, Peet MM, Karunakaran D, Grasperge B, Dobek G, Cain CM, Hope T, Kiser PF. A Subcutaneous Implant of Tenofovir Alafenamide Fumarate Causes Local Inflammation and Tissue Necrosis in Rabbits and Macaques. Antimicrob Agents Chemother. 2020 Feb 21;64(3):e01893-19. doi: 10.1128/AAC.01893-19. PMID: 31871073; PMCID: PMC7038301.

In vivo study

2. Su JT, Simpson SM, Sung S, Tfaily EB, Veazey R, Marzinke M, Qiu J, Watrous D, Widanapathirana L, Pearson E, Peet MM, Karunakaran D, Grasperge B, Dobek G, Cain CM, Hope T, Kiser PF. A Subcutaneous Implant of Tenofovir Alafenamide Fumarate Causes Local Inflammation and Tissue Necrosis in Rabbits and Macaques. Antimicrob Agents Chemother. 2020 Feb 21;64(3):e01893-19. doi: 10.1128/AAC.01893-19. PMID: 31871073; PMCID: PMC7038301.
2. Zane D, Roller S, Shelton J, Singh R, Jain R, Wang Y, Yang B, Felx M, Alessi T, Feldman PL. A 28-Day Toxicity Study of Tenofovir Alafenamide Hemifumarate by Subcutaneous Infusion in Rats and Dogs. Microbiol Spectr. 2021 Jun 30:e0033921. doi: 10.1128/Spectrum.00339-21. Epub ahead of print. PMID: 34190595.

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7. Bioactivity

Biological target:

Tenofovir alafenamide hemifumarate (GS-7340 hemifumarate) is an investigational oral prodrug of Tenofovir, which is a HIV-1 nucleotide reverse transcriptase inhibitor.

In vitro activity

TAF (tenofovir alafenamide hemifumarate) reservoir implants were formed by compressing the TAF drug substance and small amounts of NaCl and magnesium stearate into a pellet that was impulse sealed into a 150- to 170-μm thin, medical-grade polyurethane tube (Fig. 1). Drug release from implants was evaluated in vitro (see Fig. S1 in the supplemental material) using the shake flask method. We observed low rates of TAF degradation (27) in phosphate-buffered saline (PBS) in in vitro release testing medium (half-life of 2.8 days at pH 7.4 at 37°C in PBS) as well as in the implant (see Supplemental 1 and 2 in the supplemental material file), although until the end of the release curve, we observed that >90% of the internal contents were in the parent form. The average TAF equivalent in vitro release rates over days 7 to 91 from the generation A implant were 0.13 mg/day for the 0.8-cm-long implants and 0.26 mg/day for the 1.6-cm-long implants, with fluxes of 0.24 mg TAF/cm2/day and 0.23 mg TAF/cm2/day, respectively. The mean TAF equivalent in vitro release rate over days 7 to 91 from the generation B implants was 0.13 mg/day, with an average flux of 0.08 mg TAF/cm2/day. In general, increases in the in vitro dose were correlated with increasing median TFV-DP concentrations.

Reference: Antimicrob Agents Chemother. 2020 Mar; 64(3): e01893-19. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7038301/

In vivo activity

The toxicity of tenofovir alafenamide (TAF) hemifumarate (HF) was evaluated when administered by continuous subcutaneous (s.c.) infusion via an external infusion pump for 28 days to rats and dogs. During the dosing period in dogs, in-life observations consisted of discharge at the infusion site with or without the presence of a skin lesion. Although infusion site reactions were observed in animals from all treatment groups, including vehicle controls, and were considered a consequence of the continuous s.c. infusion model, the frequency and severity of the reactions and associated observations were greater in TAF-treated animals, suggesting that infusion site reactions were exacerbated by administration of TAF HF. Administration of TAF HF to rats elicited changes in hematology parameters at a dose of ⩾30 μg/kg/day. These changes included increases in white blood cell counts (WBC), neutrophil counts (NEUT), lymphocyte counts (LYMPH), monocyte counts (MONO), eosinophil counts (EOS), and platelet counts (PLT). Administration of TAF HF to rats was associated with minimal changes in clinical chemistry parameters at doses of ⩾30 μg/kg/day. Alterations occurred in alkaline phosphatase activity (ALP), glucose (GLUC), total protein (TPROT), albumin (ALB), globulin (GLOB), albumin/globulin ratio (A/G ratio), and urea nitrogen (UREAN) concentrations. The main finding in this study is that TAF HF administered continuously as a s.c. infusion appears to exacerbate a background inflammation response to the presence of the s.c. catheter (foreign body response) in the tissue surrounding the infusion site in rats and dogs at all doses tested after 28 days of administration.

Reference: Microbiol Spectr. 2021 Jun 30:e0033921. https://journals.asm.org/doi/10.1128/Spectrum.00339-21