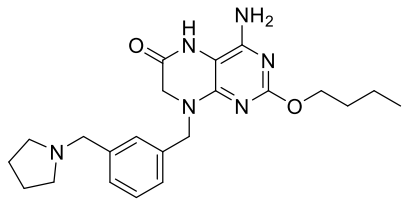
Product data sheet

MedKoo Cat#: 206456 Name: Vesatolimod CAS#: 1228585-88-3 Chemical Formula: $C_{22}H_{30}N_6O_2$ Exact Mass: 410.24302 Molecular Weight: 410.52	
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:
Vesatolimod, also known as GS-9620, is a potent and oral agonist of Toll-like receptor-7 developed for finite treatment of chronic hepatitis B viral (HBV) infection, with the goal of inducing a liver-targeted antiviral effect without inducing the adverse effects associated with current systemic interferon-α (IFN-α) therapies. GS-9620 demonstrate interferon-stimulated gene induction without detectable serum interferon at low oral doses. GS-9620 can induce a sustained antiviral response in the woodchuck model of CHB.

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	10.89	26.53
DMSO:PBS (pH 7.2) (1:3)	0.25	0.61
DMF	1.0	2.44
4-methylpyridine	12.0	29.23

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.44 mL	12.18 mL	24.36 mL
5 mM	0.49 mL	2.44 mL	4.87 mL
10 mM	0.24 mL	1.22 mL	2.44 mL
50 mM	0.05 mL	0.24 mL	0.49 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. Tsai A, Irrinki A, Kaur J, Cihlar T, Kukolj G, Sloan DD, Murry JP. Toll-Like Receptor 7 Agonist GS-9620 Induces HIV Expression and HIV-Specific Immunity in Cells from HIV-Infected Individuals on Suppressive Antiretroviral Therapy. J Virol. 2017 Mar 29;91(8):e02166-16. doi: 10.1128/JVI.02166-16. PMID: 28179531; PMCID: PMC5375698.
2. Bam RA, Hansen D, Irrinki A, Mulato A, Jones GS, Hesselgesser J, Frey CR, Cihlar T, Yant SR. TLR7 Agonist GS-9620 Is a Potent Inhibitor of Acute HIV-1 Infection in Human Peripheral Blood Mononuclear Cells. Antimicrob Agents Chemother. 2016 Dec 27;61(1):e01369-16. doi: 10.1128/AAC.01369-16. PMID: 27799218; PMCID: PMC5192112.

In vivo study

1. Menne S, Tumas DB, Liu KH, Thampi L, AlDeghaither D, Baldwin BH, Bellezza CA, Cote PJ, Zheng J, Halcomb R, Fosdick A, Fletcher SP, Daffis S, Li L, Yue P, Wolfgang GH, Tennant BC. Sustained efficacy and seroconversion with the Toll-like receptor 7

agonist GS-9620 in the Woodchuck model of chronic hepatitis B. J Hepatol. 2015 Jun;62(6):1237-45. doi: 10.1016/j.jhep.2014.12.026. Epub 2015 Jan 2. PMID: 25559326; PMCID: PMC4439359.
2. Lanford RE, Guerra B, Chavez D, Giavedoni L, Hodara VL, Brasky KM, Fosdick A, Frey CR, Zheng J, Wolfgang G, Halcomb RL, Tumas DB. GS-9620, an oral agonist of Toll-like receptor-7, induces prolonged suppression of hepatitis B virus in chronically infected chimpanzees. Gastroenterology. 2013 Jun;144(7):1508-17, 1517.e1-10. doi: 10.1053/j.gastro.2013.02.003. Epub 2013 Feb 13. PMID: 23415804; PMCID: PMC3691056.

7. Bioactivity

Biological target:

Vesatolimod (GS-9620) is an agonist of Toll-Like Receptor (TLR7) with an EC50 of 291 nM.

In vitro activity

As shown in Table 1, GS-9620 was inactive against HIV in isolated $CD4^+$ T cells and macrophages up to the highest concentration tested (10 μM) but did show dose-dependent inhibition of HIV-1 replication in complete PBMCs following infection with either HIV-1_{BaL} (EC_{50} = 536 nM) or HIV-$1_{VSV\text{-}G\text{-}LUC}$ (EC_{50} = 953 nM). Although GS-9620-mediated antiretroviral activity varied significantly between individual donors, its antiretroviral potency in PBMCs was enhanced by approximately 35-fold when GS-9620 was added 48 h prior to infection with HIV-$1_{VSV\text{-}G\text{-}LUC}$ (EC_{50} = 27 nM). Similar potency improvements were also observed in GS-9620-pretreated PBMCs infected with HIV-1_{BaL} (data not shown). The antiretroviral activity was likely not due to cytotoxicity. A 50% cytotoxic concentration (CC_{50}) value of 22 μM for uninfected activated PBMCs translates to a mean selectivity index (CC_{50}/EC_{50} ratio) of 815-fold for GS-9620.

Reference: Antimicrob Agents Chemother. 2017 Jan; 61(1): e01369-16. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5192112/

In vivo activity

GS-9620 treatment induced marked, sustained reductions in serum WHV DNA noted as early as the first week of treatment. GS-9620 induced reductions in viremia occurred in nearly all GS-9620-treated woodchucks by week 4 (Fig. 3 and Table 2). In contrast, the placebo group had no changes in serum WHV DNA. WHV-infected woodchucks treated QOD for 4 weeks (group 3) had a uniformly marked antiviral response with a mean maximal viral load reduction of 6.2 $\log_{10}$. At the end of the study (week 35), this group had a mean 4.8 $\log_{10}$ reduction in viral load. Mean viral load in this group during weeks 3–35 were significantly reduced compared to pretreatment (all $p<0.05$) and the placebo control group at weeks 2–35 (all $p<0.05$).

Reference: J Hepatol. 2015 Jun; 62(6): 1237–1245. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4439359/