

Product data sheet



MedKoo Cat#: 561151 Name: E6446 CAS#: 1219925-73-1 (free base) Chemical Formula: C ₂₇ H ₃₅ N ₃ O ₃ Exact Mass: 449.2678 Molecular Weight: 449.595	
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:

E6446 inhibits Toll-like receptor (TLR)7 and 9 signaling. E6446 works in a variety of human and mouse cell types and inhibits DNA-TLR9 interaction in vitro. When administered to mice, this compound suppresses responses to challenge doses of cytidine-phosphate-guanidine (CpG)-containing DNA, which stimulates TLR9.

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
Ethanol	90.0	200.18

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.22 mL	11.12 mL	22.24 mL
5 mM	0.44 mL	2.22 mL	4.45 mL
10 mM	0.22 mL	1.11 mL	2.22 mL
50 mM	0.04 mL	0.22 mL	0.44 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. Ueda H, Yamaguchi O, Taneike M, Akazawa Y, Wada-Kobayashi H, Sugihara R, Yorifuji H, Nakayama H, Omiya S, Murakawa T, Sakata Y, Otsu K. Administration of a TLR9 Inhibitor Attenuates the Development and Progression of Heart Failure in Mice. *JACC Basic Transl Sci.* 2019 May 22;4(3):348-363. doi: 10.1016/j.jacbts.2019.01.002. PMID: 31312759; PMCID: PMC6610159.
2. Franklin BS, Ishizaka ST, Lamphier M, Gusovsky F, Hansen H, Rose J, Zheng W, Ataíde MA, de Oliveira RB, Golenbock DT, Gazzinelli RT. Therapeutic targeting of nucleic acid-sensing Toll-like receptors prevents experimental cerebral malaria. *Proc Natl Acad Sci U S A.* 2011 Mar 1;108(9):3689-94. doi: 10.1073/pnas.1015406108. Epub 2011 Feb 8. PMID: 21303985; PMCID: PMC3048158.

In vivo study

1. Ueda H, Yamaguchi O, Taneike M, Akazawa Y, Wada-Kobayashi H, Sugihara R, Yorifuji H, Nakayama H, Omiya S, Murakawa T, Sakata Y, Otsu K. Administration of a TLR9 Inhibitor Attenuates the Development and Progression of Heart Failure in Mice. *JACC Basic Transl Sci.* 2019 May 22;4(3):348-363. doi: 10.1016/j.jacbts.2019.01.002. PMID: 31312759; PMCID: PMC6610159.
2. Yoshida K, Abe K, Ishikawa M, Saku K, Shinoda-Sakamoto M, Ishikawa T, Watanabe T, Oka M, Sunagawa K, Tsutsui H. Inhibition of TLR9-NF-κB-mediated sterile inflammation improves pressure overload-induced right ventricular dysfunction in rats. *Cardiovasc Res.* 2019 Mar 1;115(3):658-668. doi: 10.1093/cvr/cvy209. PMID: 30239623.

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7. Bioactivity

Biological target:

E6446 is an inhibitor of Toll-like receptor (TLR) 7 and 9 signaling in a variety of human and mouse cell types and inhibits DNA-TLR9 interaction in vitro.

In vitro activity

Measurement of ELAM-1-luciferase activity showed that E6446 specifically inhibited TLR9 activation with CpG ODN 2006, in the range of 0.01–0.03 μM . A 100-fold higher concentration (2–8 μM) of E6446 was required to inhibit TLR7/8 activated by the imidazoquinoline compound R848. Incubation of cells with even higher concentrations (30 μM) of E6446 was required to reduce 50% of TLR4 activation (Fig. 2A).

Reference: Proc Natl Acad Sci U S A. 2011 Mar 1; 108(9): 3689–3694. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3048158/>

In vivo activity

E6446 treatment significantly reduced LV chamber size and improved cardiac function in TAC-operated mice.

Reference: JACC Basic Transl Sci. 2019 Jun; 4(3): 348–363. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6610159/>

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.