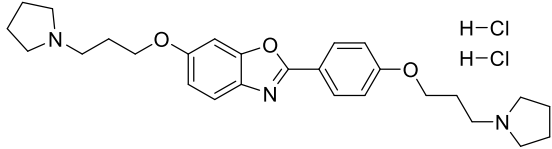


Product data sheet



MedKoo Cat#: 555222 Name: E6446 HCl CAS#: 1345675-25-3 (HCl) Chemical Formula: C ₂₇ H ₃₇ Cl ₂ N ₃ O ₃ Molecular Weight: 522.511		
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 is a synthetic antagonist of nucleic acid-sensing TLRs. In vitro, low doses of E6446 specifically inhibited the activation of human and mouse TLR9. Tenfold higher concentrations of this compound also inhibited the human TLR8 response to single-stranded RNA. In vivo, therapy with E6446 diminished the activation of TLR9 and prevented the exacerbated cytokine response observed during acute Plasmodium infection. Furthermore, severe signs of ECM, such as limb paralysis, brain vascular leak, and death, were all prevented by oral treatment with E6446.

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	7.5	14.35
DMF	20.0	38.28
DMF:PBS (pH 7.2) (1:4)	0.2	0.38
Ethanol	2.0	3.83
Water	100.0	191.38

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.91 mL	9.57 mL	19.14 mL
5 mM	0.38 mL	1.91 mL	3.83 mL
10 mM	0.19 mL	0.96 mL	1.91 mL
50 mM	0.04 mL	0.19 mL	0.38 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. Therapeutical 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

Product data sheet



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- κ B-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.

7. Bioactivity

Biological target:

E6446 dihydrochloride is a specific Toll-like receptor 9 inhibitor.

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 μ M. A 100-fold higher concentration (2–8 μ M) of E6446 was required to inhibit TLR7/8 activated by the imidazoquinoline compound R848. Incubation of cells with even higher concentrations (30 μ M) 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.