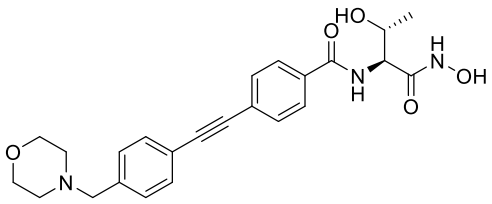
Product data sheet

MedKoo Cat#: 526733 Name: CHIR-090 CAS#: 728865-23-4 Chemical Formula: $C_{24}H_{27}N_3O_5$ Exact Mass: 437.1951 Molecular Weight: 437.496	
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:

CHIR-090 is a very potent and selective LpxC inhibitor. CHIR-090 has excellent antibiotic activity against Pseudomonas aeruginosa and Escherichia coli. CHIR-090 is also a two-step slow, tight-binding inhibitor of E. coli LpxC with Ki = 4.0 nM, Ki* = 0.5 nM, k5 = 1.9 min-1, and k6 = 0.18 min-1. CHIR-090 at low nanomolar levels inhibits LpxC orthologues from diverse Gram-negative pathogens, including P. aeruginosa, Neisseria meningitidis, and Helicobacter pylori. In contrast, CHIR-090 is a relatively weak competitive and conventional inhibitor (lacking slow, tight-binding kinetics) of LpxC from Rhizobium leguminosarum (Ki = 340 nM), a Gram-negative plant endosymbiont that is resistant to this compound. CHIR-090 is an excellent lead for the further development of new antibiotics targeting the lipid A pathway.

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	3.75	8.57
DMF	2.0	4.57

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.29 mL	11.43 mL	22.86 mL
5 mM	0.46 mL	2.29 mL	4.57 mL
10 mM	0.23 mL	1.14 mL	2.29 mL
50 mM	0.05 mL	0.23 mL	0.46 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. Hou F, Chang Y, Huang Z, Han N, Bin L, Deng H, Li Z, Pan Z, Ding L, Gao H, Yang R, Zhi F, Bi Y. Application of LpxC enzyme inhibitor to inhibit some fast-growing bacteria in human gut bacterial culturomics. BMC Microbiol. 2019 Dec 30;19(1):308. doi: 10.1186/s12866-019-1681-6. PMID: 31888576; PMCID: PMC6937742.

2. Richie DL, Takeoka KT, Bojkovic J, Metzger LE 4th, Rath CM, Sawyer WS, Wei JR, Dean CR. Toxic Accumulation of LPS Pathway Intermediates Underlies the Requirement of LpxH for Growth of Acinetobacter baumannii ATCC 19606. PLoS One. 2016 Aug 15;11(8):e0160918. doi: 10.1371/journal.pone.0160918. PMID: 27526195; PMCID: PMC4985137.

In vivo study

1. Tan JH, Vidaillac C, Yam JKH, Chua SL, Givskov M, Yang L. In Vitro and In Vivo Efficacy of an LpxC Inhibitor, CHIR-090, Alone or Combined with Colistin against Pseudomonas aeruginosa Biofilm. Antimicrob Agents Chemother. 2017 Jun 27;61(7):e02223-16. doi: 10.1128/AAC.02223-16. PMID: 28461320; PMCID: PMC5487635.

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7. Bioactivity

Biological target:

CHIR-090 is a slow, tight-binding inhibitor of the LpxC deacetylase with a Ki of 4.0 nM for *E. coli* LpxC.

In vitro activity

Strongly supporting this notion, growth of LpxH depleted cells (-IPTG) was rescued by exposure to the well-characterized LpxC inhibitor, CHIR-090 in a dose-dependent fashion (Fig 7A and 7B). The concentration of CHIR-090 used here (8–16 μg/ml) was sufficient to block LpxC since this level of exposure dramatically reduces or eliminates LPS production in A. baumannii ATCC19606 (S20 Fig). A similar result was recently reported using the LpxC inhibitor PF-508109 at 32 μg/ml. Furthermore, cells under LpxH depletion conditions in the presence of CHIR-090 had much lower accumulation these pathway intermediates, indicating that the synthesis of these intermediates was blocked by CHIR-090 under these growth conditions (Fig 8A–8F). These data strongly indicate that toxic accumulation of one or more lipid A pathway intermediates underlies the dependence on LpxH for growth of A. baumannii ATCC 19606.

Reference: PLoS One. 2016; 11(8): e0160918. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4985137/

In vivo activity

The *in vivo* efficacy of colistin and CHIR-090, alone and in combination, was evaluated using a mouse implant model of infection. The results are presented in Fig. 3. Both in the implant and in the spleen, similar log counts were observed for the mice from the control group (treated with DMSO) and the untreated group (treated with 0.9% NaCl) (Fig. 3). For both the implant and spleen, CHIR-090 used as monotherapy resulted in an approximately 2-$\log_{10}$ kill, whereas colistin caused a 3-$\log_{10}$ reduction compared to the counts in the untreated or control group (Fig. 3). The combination of colistin and CHIR-090 resulted in a greater reduction in the number of CFU (up to 4 $\log_{10}$) (Fig. 3).

Reference: Antimicrob Agents Chemother. 2017 Jul; 61(7): e02223-16. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5487635/

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.