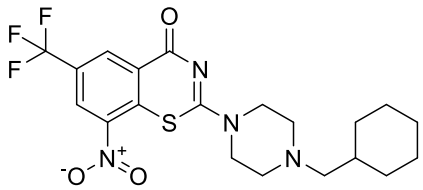
Product data sheet

MedKoo Cat#: 522563 Name: PBTZ169 CAS#: 1377239-83-2 Chemical Formula: $C_{20}H_{23}F_3N_4O_3S$ Exact Mass: 456.1443 Molecular Weight: 456.48	
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:

PBTZ169, also known as macozinone, is a new drug candidate that inhibits decaprenyl-phosphoribose-epimerase (DprE1), an essential enzyme involved in the cell wall biosynthesis of Corynebacterineae. The MIC values of PBTZ169 ranged from 0.03 μg/mL to 0.0037 μg/mL. The MIC50 and MIC90 values of PBTZ169 were 0.0075 and 0.030 μg/mL, respectively. The MIC for PBTZ169 for N. brasiliensis HUJEG-1 was 0.0037 μg/mL. The MICs of SXT, DA-7218, and BTZ043 for this strain were 9.5/0.5, 8, and 0.125 μg/mL, respectively.

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	4.6	10.1

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.19 mL	10.95 mL	21.91 mL
5 mM	0.44 mL	2.19 mL	4.38 mL
10 mM	0.22 mL	1.10 mL	2.19 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. Spaggiari D, Desfontaine V, Cruchon S, Guinchard S, Vocat A, Blattes E, Pitteloud J, Ciullini L, Bardinet C, Ivanyuk A, Makarov V, Ryabova O, Buclin T, Cole ST, Decosterd LA. Development and validation of a multiplex UHPLC-MS/MS method for the determination of the investigational antibiotic against multi-resistant tuberculosis macozinone (PBTZ169) and five active metabolites in human plasma. PLoS One. 2019 May 31;14(5):e0217139. doi: 10.1371/journal.pone.0217139. PMID: 31150423; PMCID: PMC6544242.
2. Shi J, Lu J, Wen S, Zong Z, Huo F, Luo J, Liang Q, Li Y, Huang H, Pang Y. In Vitro Activity of PBTZ169 against Multiple Mycobacterium Species. Antimicrob Agents Chemother. 2018 Oct 24;62(11):e01314-18. doi: 10.1128/AAC.01314-18. PMID: 30150479; PMCID: PMC6201125.

In vivo study

1. Lupien A, Vocat A, Foo CS, Blattes E, Gillon JY, Makarov V, Cole ST. Optimized Background Regimen for Treatment of Active Tuberculosis with the Next-Generation Benzothiazinone Macozinone (PBTZ169). Antimicrob Agents Chemother. 2018 Oct 24;62(11):e00840-18. doi: 10.1128/AAC.00840-18. PMID: 30126954; PMCID: PMC6201121.

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2. González-Martínez NA, Lozano-Garza HG, Castro-Garza J, De Osio-Cortez A, Vargas-Villarreal J, Cavazos-Rocha N, Ocampo-Candiani J, Makarov V, Cole ST, Vera-Cabrera L. In Vivo Activity of the Benzothiazinones PBTZ169 and BTZ043 against Nocardia brasiliensis. PLoS Negl Trop Dis. 2015 Oct 16;9(10):e0004022. doi: 10.1371/journal.pntd.0004022. PMID: 26474057; PMCID: PMC4608729.

7. Bioactivity

Biological target:

Macozinone (PBTZ169) is a bactericidal benzothiazinone and a potent DprE1 (decaprenylphosphoryl-β-d-ribose 2'-oxidase) inhibitor.

In vitro activity

The most important finding of this study is that PBTZ169 exhibits excellent in vitro activity against MDR-TB and XDR-TB. All M. tuberculosis isolates tested have an MIC of less than 0.25 mg/liter, the MIC90 of which is significantly lower than those of moxifloxacin (16.0 mg/liter), linezolid (1.0 mg/liter), and clofazimine (1.0 mg/liter), while similar to those of bedaquiline (0.031 mg/liter) and delamanid (0.031 mg/liter) (18). Despite the limited data regarding plasma concentration of PBTZ169, the extremely low MICs against MDR-TB and XDR-TB highlight the promising efficacy of this anti-TB agent as part of a treatment for pulmonary MDR-TB and XDR-TB.

Reference: Antimicrob Agents Chemother. 2018 Nov; 62(11): e01314-18. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6201125/

In vivo activity

Thus, the in vivo activity of these two drugs was evaluated in a mouse TB model (Fig. 2). At the concentrations tested, all drugs alone and in combinations significantly decreased the bacterial burden by more than 2.18 $\log_{10}$ in the lungs and 1.71 $\log_{10}$ in the spleens compared to the level on day 0, thus indicating a bactericidal effect. Although no combinatory effect was observed in these organs when MCZ (macozinone), DMD (delamanid), and STZ (sutezolid) were combined in two-drug combinations, the triple combination MCZ-DMD-STZ was more active in the lungs of M. tuberculosis-infected mice than DMD-STZ (the most active of the two-drug combinations) with bactericidal activity of more than 0.69 $\log_{10}$ CFU ($P = 0.014$).

Reference: Antimicrob Agents Chemother. 2018 Nov; 62(11): e00840-18. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6201121/

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.