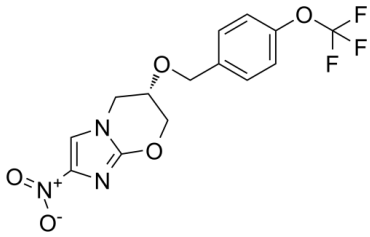
Data Sheet

Product Name:	Pretomanid
Cat. No.:	CS-3090
CAS No.:	187235-37-6
Molecular Formula:	C14H12F3N3O5
Molecular Weight:	359.26
Target:	Bacterial
Pathway:	Anti-infection
Solubility:	DMSO : 20 mg/mL (55.67 mM; ultrasonic and warming and heat to 80°C)



BIOLOGICAL ACTIVITY:

Pretomanid (PA-824) is a small-molecule nitroimidazopyran drug candidate for the treatment of tuberculosis; the MIC values of PA-824 against a panel of MTB pan-sensitive and rifampin mono-resistant clinical isolates ranged from 0.015 to 0.25 ug/ml. IC50 value: 0.015 to 0.25 ug/ml (MICs) [1] IC50 & Target: Tuberculosis. **In Vitro:** Pretomanid (PA-824) exhibited a sub-micromolar minimal inhibitory concentration (MIC) against MTB, Although Pretomanid (PA-824) was not the most potent NAP against cultured MTB clinical isolates, it was the most active in infected mice when orally administered at 25 mg/kg. This indicated that Pretomanid (PA-824) might possess more desirable pharmacokinetic properties than the other more potent NAP compounds that we tested. Further studies in mice at 25, 50 and 100 mg kg-1 Pretomanid (PA-824) daily for 10 days resulted in reductions of mycobacterial burden in both spleen and lung tissues that were comparable to that of INH at 25 mg kg -1 [1]. Pretomanid (PA-824) showed significant activity at 2, 10, and 50 microg/ml, similar to that of metronidazole, in a dose-dependent manner. Pretomanid (PA-824) at 100 mg/kg in cyclodextrin/lecithin was as active as moxifloxacin at 100 mg/kg and isoniazid at 25 mg/kg and was slightly more active than rifampin at 20 mg/kg. Long-term treatment with Pretomanid (PA-824) at 100 mg/kg in cyclodextrin/lecithin reduced the bacterial load below 500 CFU in the lungs and spleen [2]. Pretomanid (PA-824) has no effect on the viability of M. leprae in all three models, consistent with the lack of the nitroimidazo-oxazine-specific nitroreductase, encoded by Rv3547 in the M. leprae genome, which is essential for activation of this molecule [3].

References:

[1]. Stover CK, et al. A small-molecule nitroimidazopyran drug candidate for the treatment of tuberculosis. Nature. 2000 Jun 22;405(6789):962-6.

[2]. Lenaerts AJ, et al. Preclinical testing of the nitroimidazopyran PA-824 for activity against Mycobacterium tuberculosis in a series of in vitro and in vivo models. Antimicrob Agents Chemother. 2005 Jun;49(6):2294-301.

[3]. Manjunatha UH, et al. Mycobacterium leprae is naturally resistant to PA-824. Antimicrob Agents Chemother. 2006 Oct;50(10):3350-4.

CAIndexNames:

5H-Imidazo[2,1-b][1,3]oxazine, 6,7-dihydro-2-nitro-6-[[4-(trifluoromethoxy)phenyl]methoxy]-, (6S)-

SMILES:

FC(F)(F)OC(C=C1)=CC=C1CO[C@@H]2COC3=NC([N+]([O-])=O)=CN3C2

Caution: Product has not been fully validated for medical applications. For research use only.

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