Product Data Sheet

Product Name: Cycloguanil D6
Cat. No.: GC39367

Chemical Properties

Cas. No.			
SMILES	ClC1=CC=C(N2C(N)=NC(N)=NC2(C([2H])([2H])[2H])C([2H])([2H])[2H])C=C1		
Formula	$C_{11}H_8D_6ClN_5$	M.Wt	257.75
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Cycloguanil D6		

Background

Cycloguanil-d_6 is intended for use as an internal standard for the quantification of cycloguanil by GC- or LC-MS. Cycloguanil is the active metabolite of the antimalarial prodrug proguanil.[1] Cycloguanil is formed from proguanil by the cytochrome P450 (CYP) isoforms CYP2C19 and CYP3A in human liver microsomes. It is an inhibitor of dihydrofolate reductase (DHFR; K_is = 1.5 and 0.79 nM for the *P. falciparum* and *P. berghei* enzymes, respectively).[2,3] It is active against ten *P. falciparum* field isolates (IC_{50}s = 0.12-1,400 ?g/ml).[2] Cycloguanil reduces parasitemia in a mouse model of *P. berghei* infection (ED_{50} = 2 mg/kg).[4] It also reduces parasitemia in a rhesus monkey model of *P. cynomolgi* infection when administered at a dose of 0.3 mg/kg.[5]

1.Birkett, D.J., Rees, D., Anderson, T., et al.In vitro proguanil activation to cycloguanil by human liver microsomes is mediated by CYP3A isoforms as well as by S-mephenytoin hydroxylaseBr. J. Clin. Pharmacol.37(5)413-420(1994) 2.Foote, S.J., Galatis, D., and Cowman, A.F.Amino acids in the dihydrofolate reductase-thymidylate synthase gene of Plasmodium falciparum involved in cycloguanil resistance differ from those involved in

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pyrimethamine resistanceProc. Natl. Acad. Sci. USA87(8)3014-3017(1990) 3.Yuthavong, Y., Vilaivan, T., Chareonsethakul, N., et al.Development of a lead inhibitor for the A16V+S108T mutant of dihydrofolate reductase from the cycloguanil-resistant strain (T9/94) of Plasmodium falciparumJ. Med. Chem.43(14)2738-2744(2000) 4.Knight, D.J., and Peters, W.The antimalarial activity of N-benzyloxydihydrotriazines. I. The activity of clociguanil (BRL 50216) against rodent malaria, and studies on its mode of actionAnn. Trop. Med. Parasitol.74(4)393-404(1980) 5.Schmidt, L.H., Loo, T.L., Fradkin, R., et al.Antimalarial activities of triazine metabolites of chlorguanide and dichlorguanideProc. Soc. Exp. Biol. Med.80(2)367-370(1952)

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