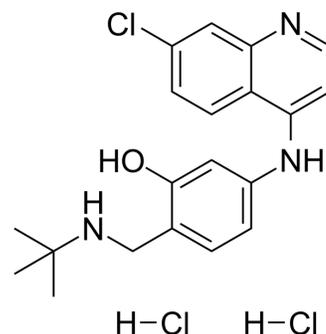


## GSK369796 Dihydrochloride

<b>Cat. No.:</b>	HY-12082A
<b>CAS No.:</b>	1010411-21-8
<b>Molecular Formula:</b>	C <sub>20</sub> H <sub>24</sub> Cl <sub>3</sub> N <sub>3</sub> O
<b>Molecular Weight:</b>	428.78
<b>Target:</b>	Potassium Channel; Parasite
<b>Pathway:</b>	Membrane Transporter/Ion Channel; Anti-infection
<b>Storage:</b>	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : 100 mg/mL (233.22 mM; Need ultrasonic)  
H<sub>2</sub>O : 50 mg/mL (116.61 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.3322 mL	11.6610 mL	23.3220 mL
	5 mM	0.4664 mL	2.3322 mL	4.6644 mL
	10 mM	0.2332 mL	1.1661 mL	2.3322 mL

Please refer to the solubility information to select the appropriate solvent.

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.5 mg/mL (5.83 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.5 mg/mL (5.83 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

GSK369796 Dihydrochloride is an affordable and effective antimalarial and inhibits hERG potassium ion channel repolarization with an IC<sub>50</sub> of 7.5 μM.

#### IC<sub>50</sub> & Target

IC<sub>50</sub>: 7.5 μM (hERG potassium ion channel)<sup>[1]</sup>

#### In Vitro

In vitro, GSK369796 Dihydrochloride can inhibit the growth of Plasmodium falciparum strains 3D7c, HB3c and K1d, with IC<sub>50</sub>s of 11.2±2.2, 12.6±5.3 and 13.2±3.2 nM, respectively. Protein binding is higher for GSK369796 Dihydrochloride (compound 4) compare to desethyl amodiaquine in the mouse (93 vs 74%) but similar in human (88 vs 86%). GSK369796 Dihydrochloride can also inhibit hERG potassium ion channel repolarization with an IC<sub>50</sub> of 7.5±0.8 μM<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

### In Vivo

In vivo, GSK369796 Dihydrochloride can inhibit the growth of Plasmodium berghei ANKA with ED<sub>50</sub> and ED<sub>90</sub> of 2.8 and 4.7 mg/kg, respectively<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

### Cell Assay <sup>[1]</sup>

Assays are performed in sterile 96-well microtiter plates, each plate contains 200 µL of parasite culture (2% parasitemia, 0.5% hematocrit) with or without 10 µL drug dilutions (including GSK369796 Dihydrochloride). Each drug is tested in triplicate and parasite growth is compared to control wells (which constitutes 100% parasite growth). Cultures are incubated for a further 24 h before they are harvested onto filter mats, dried for 1 h at 55 °C, and counted. IC<sub>50</sub> values are calculated<sup>[1]</sup>.

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### Animal Administration <sup>[1]</sup>

The efficacy of selected 4-aminoquinolines (including GSK369796 Dihydrochloride) is measured against *P. yoelii* or *P. berghei* in a 4-day test. 28 Cohorts of age-matched female mice are infected iv with 6.4×10<sup>6</sup> or 10.0×10<sup>6</sup> parasites obtained from infected donors, and the mice are randomly distributed in groups of n=5 mice/group (day 0). Treatments are administered from day 0 (one hour after infection) until day 3. The therapeutic efficacy of compounds (including GSK369796 Dihydrochloride) is expressed as the effective dose that reduces parasitemia by 50% (ED<sub>50</sub>) and 90% (ED<sub>90</sub>) with respect to vehicle treated groups (ED<sub>90</sub>) and the dose that achieved eradication of parasitemia until day 23 after infection (NRL). All compounds (including GSK369796 Dihydrochloride) and corresponding vehicles are administered orally at 20 mg/kg or subcutaneously at 10 mg/kg, as appropriate<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## REFERENCES

[1]. O'Neill PM, et al. Candidate selection and preclinical evaluation of N-tert-butyl isoquine (GSK369796), an affordable and effective 4-aminoquinoline antimalarial for the 21st century. *J Med Chem.* 2009 Mar 12;52(5):1408-15.

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

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