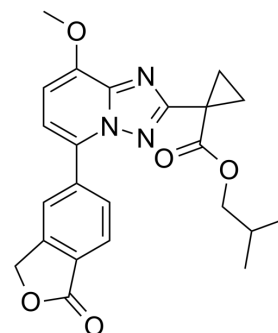


## LEO 39652

<b>Cat. No.:</b>	HY-131707		
<b>CAS No.:</b>	1445656-91-6		
<b>Molecular Formula:</b>	C <sub>23</sub> H <sub>23</sub> N <sub>3</sub> O <sub>5</sub>		
<b>Molecular Weight:</b>	421.45		
<b>Target:</b>	Phosphodiesterase (PDE)		
<b>Pathway:</b>	Metabolic Enzyme/Protease		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : 25 mg/mL (59.32 mM; Need ultrasonic)

Concentration	Mass		
	1 mg	5 mg	10 mg
<b>1 mM</b>	2.3728 mL	11.8638 mL	23.7276 mL
<b>5 mM</b>	0.4746 mL	2.3728 mL	4.7455 mL
<b>10 mM</b>	0.2373 mL	1.1864 mL	2.3728 mL

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

### BIOLOGICAL ACTIVITY

#### Description

LEO 39652 is a dual-soft PDE4 inhibitor with IC<sub>50</sub>s of 1.2 nM, 1.2 nM, 3.0 nM and 3.8 nM for PDE4A, PDE4B, PDE4C and PDE4D, respectively. LEO 39652 also inhibits TNF-α with an IC<sub>50</sub> value of 6.0 nM. LEO 39652 is used for topical research of Atopic dermatitis (AD) [1].

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

PDE4D 3.8 nM (IC <sub>50</sub> )	TNF-α 6.0 nM (IC <sub>50</sub> )	PDE4A 1.2 nM (IC <sub>50</sub> )	PDE4B 1.2 nM (IC <sub>50</sub> )
PDE4C2 3.0 nM (IC <sub>50</sub> )			

#### In Vitro

LEO 39652 shows unbound in vitro potency when measured as LPS induced TNF-α release in human peripheral blood mononuclear cells (PBMC), incubated in serum free medium. LEO 39652 shows a relatively high binding to human serum albumin[2].  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**In Vivo**

LEO 39652 is inactivated both in blood and liver (dual-soft) while stabled in the skin<sup>[1]</sup>. Pharmacokinetic Analysis LEO 39652 exhibits total clearance (rats 930, minipigs 200 and monkey 300 mL/min/kg) and ratio to total AUC (rats 4, minipigs 6 and monkey 6 %) following intravenous administration (rats 0.075, minipigs 0.5 and monkeys 2.0 mg/kg)<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	3 male Sprague Dawley rats, 2 female Göttingen minipigs, 2 male Göttingen minipigs, 2 female cynomolgus monkeys and 2 male cynomolgus monkeys <sup>[1]</sup>
Dosage:	Rats 0.075, minipigs 0.5 and monkeys 2.0 mg/kg
Administration:	Intravenous injection
Result:	Total clearance of 930, 200 and 300 mL/min/kg for rats, minipigs and monkeys, respectively.

**REFERENCES**

[1]. Jens Larsen, et al. Discovery and Early Clinical Development of Isobutyl 1-[8-Methoxy-5-(1-oxo-3 H-isobenzofuran-5-yl)-[1,2,4]triazolo[1,5- a]pyridin-2-yl]cyclopropanecarboxylate (LEO 39652), a Novel "Dual-Soft" PDE4 Inhibitor for Topical Treatment of Ato

[2]. Stefan Eirefelt, et al. Evaluating Dermal Pharmacokinetics and Pharmacodynamic Effect of Soft Topical PDE4 Inhibitors: Open Flow Microperfusion and Skin Biopsies. Pharm Res. 2020 Nov 13;37(12):243.

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

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