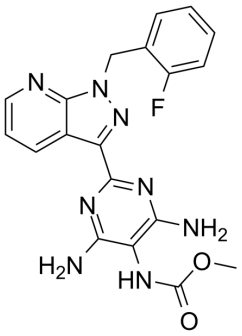
Nelociguat

Cat. No.:	HY-78237
CAS No.:	625115-52-8
Molecular Formula:	$C_{19}H_{17}FN_8O_2$
Molecular Weight:	408.39
Target:	Guanylate Cyclase
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro	DMSO : < 1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble or slightly soluble)
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.08 mg/mL (5.09 mM); Clear solution 2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (5.09 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Nelociguat (BAY60-4552) is a nitric oxide sensitive soluble guanylate cyclase stimulator.
In Vitro	Soluble guanylate cyclase (sGC) is a key enzyme in the nitric oxide (NO) signalling pathway[1]. Riociguat is metabolized to BAY60-4552 not only via cytochrome P450 isoenzymes 3A4 (CYP3A4), CYP2C8, and CYP2J2, but also via CYP1A1, located in the liver and lungs[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GSK2181236A and BAY 60-4552 provide partial benefit against hypertension-induced end-organ damage. In spontaneously hypertensive stroke-prone rats, a low dose of BAY 60-4552 decreases urine output and improved survival. A high dose also reduces urine output, and in addition reduces microalbuminuria and attenuates the increase in mean arterial pressure. Both the 0.3 and 3 mg/kg/day doses of BAY 60-4552 improves survival of 46 and 69%. Seven weeks of treatment with BAY 60-4552 (0.3 and 3.0 mg/kg/day) dose-dependently decreases urine output to 79±11 and 56±10 mL/day[1]. BAY 60-4552, and vardenafil provides synergistic beneficial effects and might therefore salvage patients who experience treatment failures with PDE5 inhibitors after radical prostatectomy[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats: Rats are orally gavaged with vehicle (0.5% HPMC, 5% DMSO, and 0.1% Tween 80; 10 mL/kg; n=14), GSK2181236A (0.1 or 1.0 mg/kg; n=11-14), or BAY 60-4552 (0.3 or 3.0 mg/kg; n=10-12) 2 h prior to ischemia. Blood is collected at the initiation of ischemia and after 24 h reperfusion. Plasma is obtained for analysis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Costell MH, et al. Comparison of soluble guanylate cyclase stimulators and activators in models of cardiovascular disease associated with oxidative stress. Front Pharmacol. 2012 Jul 5;3:128.

[2]. Zhao X, et al. Pharmacokinetics of the Soluble Guanylate Cyclase Stimulator Riociguat in Healthy Young Chinese Male Non-Smokers and Smokers: Results of a Randomized, Double-Blind, Placebo-Controlled Study. Clin Pharmacokinet. 2016 May;55(5):615-24.

[3]. Oudot A, et al. Combination of BAY 60-4552 and vardenafil exerts proerectile facilitator effects in rats with cavernous nerve injury: a proof of concept study for the treatment of phosphodiesterase type 5 inhibitor failure. Eur Urol. 2011 Nov;60(5):1020-6

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