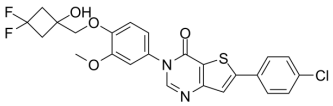
BMS-814580

Cat. No.:	HY-120608
CAS No.:	1197420-11-3
Molecular Formula:	$C_{24}H_{19}ClF_2N_2O_4S$
Molecular Weight:	504.93
Target:	MCHR1 (GPR24)
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	BMS-814580 is an orally active, highly efficacious MCHR1 inhibitor with a K_i of 16.9 nM against hMCHR1. BMS-814580 shows antiobesity activities[1].
IC_{50} & Target	K_i: 16.9 nM (MCHR1)[1]
In Vitro	BMS-814580 (3.0 μM; 10 min) shows stability with 90%, 95% and 100% remaining in human, rat and mouse liver microsomes, respectively[1]. BMS-814580 displays modest in vitro ion channel inhibition of 43%, 21%, and 15%, respectively, for hERG, Na (4 Hz), and L-type Ca channels at 10 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	BMS-814580 (0-3 mg/kg; p.o.; once daily for 28 days) shows antiobesity activities in rats[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Obese male SD rats, chronic diet-induced obese (DIO) rat model[1]
Dosage:	0.03, 0.1, 0.3, 1 and 3 mg/kg
Administration:	Orally administered as the phosphate prodrug, once daily for 28 days
Result:	Dose dependently reduced body weight.

Animal Model:	Sprague-Dawley Rats[1]
Dosage:	10 mg/kg
Administration:	Oral administration, once
Result:	Pharmacokinetics (PK) and Pharmacodynamics (PD) Data: Plasma and Brain Concentrations of Cyclic Tertiary Alcohols and the Effect on Body Weights in Sprague-Dawley Rats

			8 h rat PK study[b]		4-day PD study[c]	day 4 parent compd	concn at 20 h
compd	dosed as[a]	AUC (μM•h)	brain (nM)	plasma (nM)	% weight loss	brain (nM)	plasma (nM)
BMS-814580	glycinate	38.1	11330	4500	6.4[d]	7955	12801

[a]Rats were dosed orally with parent compound or a prodrug; prodrugs doses were adjusted to parent compounds. Vehicle = 0.5% Methocel, 0.1% Tween 80, 99.4% distilled water. [b]Dose = 10 mg/kg; plasma and brain concentrations are reported 8 h after dose, n = 2. [c]Compounds were dosed at 3, 10, and 30 mg/kg orally once a day for 4 days; weight loss data is reported only for the 10 mg/kg dose, n = 8; reduction in body weight is reported as % change from baseline body weight compared to vehicle treated animals. NT = not tested. [d]No biliary lesions were seen in this model.

Animal Model:	Sprague-Dawley Rats[1]
Dosage:	10 mg/kg (phosphate prodrug) or 1 mg/kg
Administration:	Oral (phosphate prodrug) or intravenous administration (Pharmacokinetic Analysis)
Result:	Pharmacokinetics Data for BMS-814580 in Rat[a]

species	compd (mg/kg)	route of admin	C_{max} (μM)	T_{max} (h)	$AUC_{0-\infty}$ (μM•h)	$T_{1/2}$ (h)	CL (mL/min/kg)	V_{ss} (L/kg)	F (%)
rat	BMS-814580 (1)	iv			11.5	>24	0.9	4.1	
	BMS-814580 phosphate (10)	po	4.0	6.7	107				54

[a]Vehicles: iv, PEG400/DMAC/water (70:5:25); po, Methocel/Tween80/water (0.5:0.1:99.4).

REFERENCES

[1]. Ahmad S, et al. Synthesis and Antiobesity Properties of 6-(4-Chlorophenyl)-3-(4-((3,3-difluoro-1-hydroxycyclobutyl)methoxy)-3-methoxyphenyl)thieno[3,2-d]pyrimidin-4(3H)-one (BMS-814580): A Highly Efficacious Melanin Concentrating Hormone Receptor 1 (MCHR1) Inhibitor. J Med Chem. 2016 Oct 13;59(19):8848-8858.

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

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