AMG9678

Cat. No.: HY-104062

CAS No.: 1159997-27-9

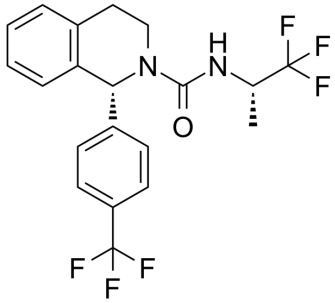
Molecular Formula: $C_{20}H_{18}F_6N_2O$

Molecular Weight: 416.36

Target: TRP Channel

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	AMG9678 is a potent, selective, orally active antagonist of TRPM8 with an IC_{50} of 31.2 nM[1].

IC_{50} & Target	TRPM8	TRPA1
	31.2 nM (IC_{50})	0.6 μM (IC_{50})

In Vitro

AMG9678 potently inhibits the menthol and cold-induced increase in intracellular calcium in cells expressing rat TRPM8, the plasma half-life ($T_{1/2}$) in rats is 7.6 h[1].

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

In Vivo

AMG9678 (0-100 mg/kg; p.o.; once) produces a significant and somewhat dose-dependent decrease in body temperature (T_b) in rats[1].

AMG9678 (30 mg/kg; p.o.; once daily for 4 consecutive days) decreases reduced body temperature after repeated dosing in rats[1].

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

Animal Model:	Male Sprague Dawley rats weighing 200–350 g (6–12 weeks of age) [1]
Dosage:	10, 30 and 100 mg/kg
Administration:	Oral administration, once or once daily for 4 consecutive days
Result:	Produced a significant and somewhat dose-dependent decrease in T_b at 10, 30 and 100 mg/kg. The magnitude of TRPM8 blockade-induced decrease in body temperature is reduced after repeated dosing. Effect of AMG9678 on T_b in rats. P value is for comparing compound administered rat T_b with vehicle administered rat T_b. End of the study plasma concentration is reported in μM. Asterisk indicates one-way ANOVA followed by Dunnett's MCT

Compound	Dose mg/kg (route)	Max T_b decrease (°C)	*P* value *	Time post dosing (min)	Plasma concentration

AMG9678	10 (p.o.)	0.72	$p < 0.001$	60	0.04 ± 0.006
AMG9678	30 (p.o.)	0.70	$p < 0.01$	60	0.34 ± 0.1
AMG9678	100 (p.o.)	0.83	$p < 0.05$	60	0.36 ± 0.12

REFERENCES

[1]. Gavva NR, et al. Transient receptor potential melastatin 8 (TRPM8) channels are involved in body temperature regulation. Mol Pain. 2012 May 9;8:36.

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