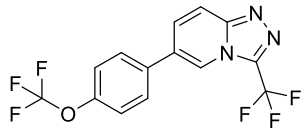
Product data sheet

MedKoo Cat#: 510345 Name: GS967 CAS#: 1262618-39-2 Chemical Formula: $C_{14}H_7F_6N_3O$ Exact Mass: 347.04933 Molecular Weight: 347.22	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
GS967, also known as GS-458967, is a highly selective late sodium channel current blocker. The selective inhibition of late INa with GS967 can exert antiarrhythmic effects by suppressing EAD- and DAD-mediated extrasystolic activity in PFs and PV and SVC sleeve preparations. Selective late INa inhibition with GS967 exerts potent protective effects against ischemia-induced depolarization and repolarization abnormalities in both atria and ventricles.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	32.5	93.60
DMF	25.0	72.0
DMF:PBS (pH 7.2) (1:2)	0.3	0.86
Ethanol	29.0	83.52

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.88 mL	14.40 mL	28.80 mL
5 mM	0.58 mL	2.88 mL	5.76 mL
10 mM	0.29 mL	1.44 mL	2.88 mL
50 mM	0.06 mL	0.29 mL	0.58 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Barbieri R, Bertelli S, Pusch M, Gavazzo P. Late sodium current blocker GS967 inhibits persistent currents induced by familial hemiplegic migraine type 3 mutations of the SCN1A gene. J Headache Pain. 2019 Nov 15;20(1):107. doi: 10.1186/s10194-019-1056-2. PMID: 31730442; PMCID: PMC6858687.
2. Ferrantini C, Pioner JM, Mazzoni L, Gentile F, Tosi B, Rossi A, Belardinelli L, Tesi C, Palandri C, Matucci R, Cerbai E, Olivotto I, Poggesi C, Mugelli A, Coppini R. Late sodium current inhibitors to treat exercise-induced obstruction in hypertrophic cardiomyopathy: an in vitro study in human myocardium. Br J Pharmacol. 2018 Jul;175(13):2635-2652. doi: 10.1111/bph.14223. Epub 2018 May 3. PMID: 29579779; PMCID: PMC6003658.

In vivo study

1. Hézső T, Naveed M, Dienes C, Kiss D, Prorok J, Árpádffy-Lovas T, Varga R, Fujii E, Mercan T, Topal L, Kistamás K, Szentandrássy N, Almássy J, Jost N, Magyar J, Bányász T, Baczkó I, Varró A, Nánási PP, Virág L, Horváth B. Mexiletine-like

cellular electrophysiological effects of GS967 in canine ventricular myocardium. Sci Rep. 2021 May 5;11(1):9565. doi: 10.1038/s41598-021-88903-3. PMID: 33953276; PMCID: PMC8100105.
2. Baker EM, Thompson CH, Hawkins NA, Wagnon JL, Wengert ER, Patel MK, George AL Jr, Meisler MH, Kearney JA. The novel sodium channel modulator GS-458967 (GS967) is an effective treatment in a mouse model of SCN8A encephalopathy. Epilepsia. 2018 Jun;59(6):1166-1176. doi: 10.1111/epi.14196. Epub 2018 May 21. PMID: 29782051; PMCID: PMC6142814.

7. Bioactivity

Biological target:

GS967 (GS458967) is an inhibitor of late I_{Na} with anti-arrhythmic actions.

In vitro activity

The application of 5 μM GS967 slightly reduced peak currents but strongly decreased persistent currents in all mutants tested (Fig. 3 b-h, i-k), while showed only a small effect on WT (Fig. 3a) overall confirming that GS967 binds directly to and interacts with the Nav1.1 protein. Scrutinizing activation and inactivation properties revealed that GS967 had no effect on activation parameters and slightly shifted the voltage of half-maximal inactivation 2–5 mV to more negative values for all mutants, except for F1774S for which GS967 shifted the half maximal inactivation voltage by about -16 mV (Additional file 1: Table S3). The most dramatic effect was seen for the process of recovery from inactivation, measured at -90 mV. While WT and all mutants fully recovered within a few ms in the absence of GS967, the drug introduced an additional, and predominant, slow component with a time constant of 400–700 ms (Fig. 4).

Reference: J Headache Pain. 2019; 20(1): 107. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6858687/

In vivo activity

In contrast, seizures in the GS967-treated *Scn8a*$^{D/+}$ mice had a single tonic phase that terminated with post-ictal suppression. Combined analysis of video-EEG and video monitoring showed that *Scn8a*$^{D/+}$ mice treated with GS967 had significantly lower seizure frequency, with 0.3 ± 0.2 seizures/24-hours in GS967-treated compared with 1.6 ± 0.4 seizures/24-hours in untreated mice ($p < 0.004$, Fig. 5C, Table 1). No seizures were observed in WT littermate mice (Table 1). These data demonstrate that GS967 has a potent anti-seizure effect in a mouse model of *SCN8A* encephalopathy.

Reference: Epilepsia. 2018 Jun; 59(6): 1166–1176. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6142814/