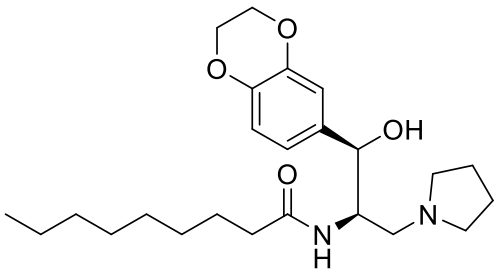
Product data sheet

MedKoo Cat#: 406141 Name: Genz-123346 CAS#: 491833-30-8 Chemical Formula: $C_{24}H_{38}N_2O_4$ Exact Mass: 418.28316 Molecular Weight: 418.57	
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:
Genz-123346 is a potent and selective glucosylceramide synthase inhibitor with potential anticancer activity. Exposure of cells to Genz-123346 and to other GCS inhibitors at non-toxic concentrations can enhance the killing of tumor cells by cytotoxic anti-cancer agents. Genz-123346 and a few other GCS inhibitors are substrates for multi-drug resistance efflux pumps such as P-gp (ABCB1, gP-170). In cell lines selected to over-express P-gp or which endogenously express P-gp, chemosensitization by Genz-123346 was primarily due to the effects on P-gp function.

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	84	200.68
Ethanol	84	200.68

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.39 mL	11.95 mL	23.89 mL
5 mM	0.48 mL	2.39 mL	4.78 mL
10 mM	0.24 mL	1.19 mL	2.39 mL
50 mM	0.05 mL	0.24 mL	0.48 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. Chai L, McLaren RP, Byrne A, Chuang WL, Huang Y, Dufault MR, Pacheco J, Madhiwalla S, Zhang X, Zhang M, Teicher BA, Carter K, Cheng SH, Leonard JP, Xiang Y, Vasconcelles M, Goldberg MA, Copeland DP, Klinger KW, Lillie J, Madden SL, Jiang YA. The chemosensitizing activity of inhibitors of glucosylceramide synthase is mediated primarily through modulation of P-gp function. Int J Oncol. 2011 Mar;38(3):701-11. doi: 10.3892/ijo.2010.888. Epub 2010 Dec 24. PMID: 21186402.

In vivo study

1. Zhao H, Przybylska M, Wu IH, Zhang J, Siegel C, Komarnitsky S, Yew NS, Cheng SH. Inhibiting glycosphingolipid synthesis improves glycemic control and insulin sensitivity in animal models of type 2 diabetes. Diabetes. 2007 May;56(5):1210-8. doi: 10.2337/db06-0719. PMID: 17470562.

2. Natoli TA, Smith LA, Rogers KA, Wang B, Komarnitsky S, Budman Y, Belenky A, Bukanov NO, Dackowski WR, Husson H, Russo RJ, Shayman JA, Ledbetter SR, Leonard JP, Ibraghimov-Beskrovnaya O. Inhibition of glucosylceramide accumulation results

in effective blockade of polycystic kidney disease in mouse models. Nat Med. 2010 Jul;16(7):788-92. doi: 10.1038/nm.2171. Epub 2010 Jun 20. PMID: 20562878; PMCID: PMC3660226.

7. Bioactivity

Biological target:

Genz-123346 is a potent, orally available glucosylceramide synthase inhibitor and inhibits GM1 with an IC50 value of 14 nM.

In vitro activity

Exposure of cells to Genz-123346 at non-toxic concentrations can enhance the killing of tumor cells by cytotoxic anti-cancer agents. This activity was unrelated to lowering intracellular glycosphingolipid levels. Genz-123346 is a substrate for multi-drug resistance efflux pumps such as P-gp (ABCB1, gP-170). In cell lines selected to over-express P-gp or which endogenously express P-gp, chemosensitization by Genz-123346 was primarily due to the effects on P-gp function.

Reference: Int J Oncol. 2011 Mar;38(3):701-11. https://www.spandidos-publications.com/ijo/38/3/701

In vivo activity

In the Zucker diabetic fatty rat, the glucosylceramide synthase inhibitor (1R,2R)-nonanoic acid[2-(2',3'-dihydro-benzo [1, 4] dioxin-6'-yl)-2-hydroxy-1-pyrrolidin-1-ylmethyl-ethyl]- amide-l-tartaric acid salt (Genz-123346) lowered glucose and A1C levels and improved glucose tolerance. Drug treatment also prevented the loss of pancreatic beta-cell function normally observed in the Zucker diabetic fatty rat and preserved the ability of the animals to secrete insulin. In the diet-induced obese mouse, treatment with Genz-123346 normalized A1C levels and improved glucose tolerance. Analysis of the phosphorylation state of the insulin receptor and downstream effectors showed increased insulin signaling in the muscles of the treated Zucker diabetic fatty rats and diet-induced obese mice.

Reference: Diabetes. 2007 May;56(5):1210-8. https://diabetes.diabetesjournals.org/lookup/pmidlookup?view=long&pmid=17470562

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.