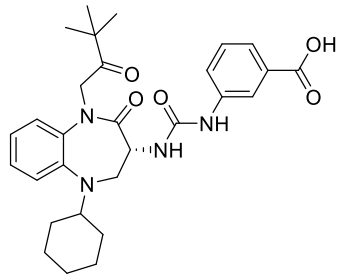
Product data sheet

MedKoo Cat#: 206018 Name: Nastorazepide (Z-360) CAS#: 209219-38-5 Chemical Formula: $C_{29}H_{36}N_4O_5$ Exact Mass: 520.26857 Molecular Weight: 520.62	
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:
Nastorazepide, also known as Z-360, is a selective, orally available, 1,5-benzodiazepine-derivative gastrin/cholecystokinin 2 (CCK-2) receptor antagonist with potential antineoplastic activity. Z-360 binds to the gastrin/CCK-2 receptor, thereby preventing receptor activation by gastrin, a peptide hormone frequently associated with the proliferation of gastrointestinal and pancreatic tumor cells.

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	61.5

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.92 mL	9.60 mL	19.21 mL
5 mM	0.38 mL	1.92 mL	3.84 mL
10 mM	0.19 mL	0.96 mL	1.92 mL
50 mM	0.04 mL	0.19 mL	0.38 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. Kawasaki D, Emori Y, Eta R, Iino Y, Hamano H, Yoshinaga K, Tanaka T, Takei M, Watson SA. Effect of Z-360, a novel orally active CCK-2/gastrin receptor antagonist on tumor growth in human pancreatic adenocarcinoma cell lines in vivo and mode of action determinations in vitro. Cancer Chemother Pharmacol. 2008 Apr;61(5):883-92. doi: 10.1007/s00280-007-0591-8. Epub 2007 Sep 28. PMID: 17901954.

In vivo study

1. Kawasaki D, Emori Y, Eta R, Iino Y, Hamano H, Yoshinaga K, Tanaka T, Takei M, Watson SA. Effect of Z-360, a novel orally active CCK-2/gastrin receptor antagonist on tumor growth in human pancreatic adenocarcinoma cell lines in vivo and mode of action determinations in vitro. Cancer Chemother Pharmacol. 2008 Apr;61(5):883-92. doi: 10.1007/s00280-007-0591-8. Epub 2007 Sep 28. PMID: 17901954.

2. Orikawa Y, Kato H, Seto K, Kobayashi N, Yoshinaga K, Hamano H, Hori Y, Meyer T, Takei M. Z-360, a novel therapeutic agent for pancreatic cancer, prevents up-regulation of ephrin B1 gene expression and phosphorylation of NR2B via suppression of interleukin-1 β production in a cancer-induced pain model in mice. Mol Pain. 2010 Oct 28;6:72. doi: 10.1186/1744-8069-6-72. PMID: 20979661; PMCID: PMC2987997.

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7. Bioactivity

Biological target:

Nastorazepide (Z-360) is a selective 1,5-benzodiazepine-derivative gastrin/cholecystokinin 2 (CCK-2) receptor antagonist.

In vitro activity

To determine the antagonistic effect of Z-360 on the CCK-2 receptor, the intracellular Ca2+ release was measured. Whereas 1 nmol/l CCK-8 increased intracellular Ca2+ release by CHO-K1/CCK-2 cells, pretreatment with Z-360F (10−11 to 10−5 mol/l) inhibited CCK-8-induced intracellular Ca2+ release in a concentration-dependent manner (IC50 value: 11 nmol/l, Fig. 3). However, Z-360F at 10−5 mol/l showed no effect on Ca2+ release in CHO-K1/CCK-2 cells without CCK-8 stimulation. As the degree of the Ca2+ release from unstimulated CHO-K1/CCK-2 cells is similar to untransfected cells (intact CHO-K1 cells), we defined as basal activity using unstimulated CHO-K1/CCK-2 cells. As Z-360F alone did not increased calcium release in CHO-K1/CCK-2 cells comparing to basal activity, it was considered that Z-360 did not act as agonist activity for classical CCK-2 receptor, at least at range of 10−5 M from 10−11 M. These results demonstrated that Z-360 shows selective antagonistic activity for the human CCK-2 receptor without an agonistic activity for CCK-2 receptor.

Reference: Cancer Chemother Pharmacol. 2008 Apr;61(5):883-92. https://dx.doi.org/10.1007/s00280-007-0591-8

In vivo activity

MiaPaCa2 cells were injected subcutaneously into the right flanks of nude mice and allowed to establish for 14 days. Z-360 was then administered orally to the mice at doses of 10, 30, or 100 mg/kg once daily for 21 days. Z-360 significantly inhibited tumor growth as measured by both tumor size (Fig. 4a) and tumor weight (Fig. 4b) in a dose-dependent manner. As shown in Fig. 4b, administration of Z-360 at 10, 30, and 100 mg/kg resulted in 16.5, 39.6, and 41.7% inhibition of final tumor weight, respectively. This dose-dependent inhibitory activity was significant at doses of 30 mg/kg ($P < 0.05$) and 100 mg/kg ($P < 0.01$).

Reference: Cancer Chemother Pharmacol. 2008 Apr;61(5):883-92. https://dx.doi.org/10.1007/s00280-007-0591-8