

## Product Data Sheet

Product Name: Zaprinst

Cat. No.: GC12909

### Chemical Properties

Cas. No. 37762-06-4

Chemical Name 5-(2-propoxyphenyl)-2H-[1,2,3]triazolo[4,5-d]pyrimidin-7(3H)-one

SMILES O=C1N=C(C2=CC=CC=C2OCCC)N=C3NNN=C31

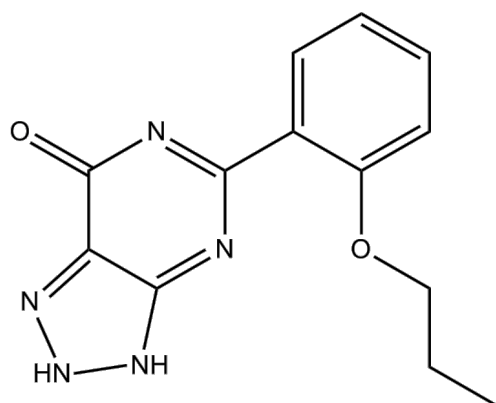
Formula  $C_{13}H_{13}N_5O_2$  M.Wt 271.28

Solubility DMF: 20 mg/ml, DMF:PBS(pH 7.2) (1:1): 0.5 mg/ml, DMSO: 10 mg/ml Storage Store at -20°C, protect from light, stored under nitrogen

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



### Protocol

#### Cell experiment [1]:

Cell lines SK-N-MC cells

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

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SK-N-MC cells were cultured in Minimum Essential Medium (MEM) supplemented with non-essential amino acid (NEAA), sodium pyruvate (110mg/l), 10% foetal bovine serum, penicillin (5000IU/ml) and streptomycin (5mg/ml), at 37°C in a humidified 5% CO<sub>2</sub> atmosphere. Cultures were

Preparation Method periodically tested for mycoplasma contamination and only negative cells were used for experiments. Cells were plated in 24-well trays at a density of  $5 \times 10^4$  cells/well. Twenty-four hours later, Zaprinst was added at various concentration (0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, and 5µM). Forty-eight hours later the number of surviving cells was determined.

Reaction Conditions 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, and 5µM; 48h

Applications Zaprinst treatment inhibited the cell viability of SK-N-MC cells in a dose-dependent manner.

### Animal experiment [2]:

Animal models LS-Mpc2<sup>-/-</sup> mice

Preparation Method LS-Mpc2<sup>-/-</sup> mice were raised in a standard sterile environment, switched from standard diet to 60% high-fat diet at 7 to 8 weeks of age and tested 12 weeks later. Zaprinst was dissolved in 25% DMSO/75% saline and administered intraperitoneally at a dose of 30mg/kg 18 hours before the glucose tolerance test (GTT).

Dosage form 30mg/kg for once; i.p.

Applications Zaprinst treatment significantly improved glucose tolerance in LS-Mpc2<sup>-/-</sup> mice.

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### References:

- [1] Giorgi M, Leonetti C, Citro G, et al. In vitro and in vivo inhibition of SK-N-MC neuroblastoma growth using cyclic nucleotide phosphodiesterase inhibitors[J]. Journal of neuro-oncology, 2001, 51(1): 25-31.
- [2] Hodges W T, Jarasvaraparn C, Ferguson D, et al. Mitochondrial pyruvate carrier inhibitors improve metabolic parameters in diet-induced obese mice[J]. Journal of Biological Chemistry, 2022, 298(2): 101554.

### Background

Zaprinast is a phosphodiesterase inhibitor that targets PDE5 and PDE6, with the IC<sub>50</sub> values of 0.8μM and 0.15μM, respectively<sup>[1]</sup>. Zaprinast acts as an agonist for rat GPR35, with a geometric mean EC<sub>50</sub> value of 16nM<sup>[2]</sup>. Through inhibition of phosphodiesterases, especially PDE5 and PDE6, Zaprinast increases intracellular cGMP levels, which modulates downstream signaling pathways such as protein kinase G (PKG) and cyclic nucleotide gated ion channels<sup>[3]</sup>. Zaprinast has been widely used in different animal models to regulate smooth muscle contraction and coronary artery relaxation<sup>[4]</sup>.

In vitro, Zaprinast treatment for 48 hours significantly inhibited SK-N-MC cell proliferation with an IC<sub>50</sub> value of 3.3μM<sup>[5]</sup>. Zaprinast (100μM) treatment for 1 hour significantly activated ERK1/2, p38 MAPK, JNK, NFκB and PI3K/Akt signaling pathways in rat microglia<sup>[6]</sup>. Pretreatment of neonatal rat-derived astrocytes with 100μM Zaprinast for 1h significantly inhibited H<sub>2</sub>O<sub>2</sub>-induced lactate dehydrogenase release and cell death<sup>[7]</sup>.

In vivo, Zaprinast treatment via intraperitoneal injection at a dose of 10mg/kg at 2 hours before and 24 and 48 hours after focal cryolesion of cortex significantly enhanced astrogliosis and reduced oxidative stress and cell death at 3 days after focal cryolesion in male Sprague-Dawley rats<sup>[8]</sup>. A single intraperitoneal injection of Zaprinast (30mg/kg) for 18 hours significantly improved glucose tolerance in diet-induced obese (DIO) mice<sup>[9]</sup>.

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- [1] Mackenzie A E, Milligan G. The emerging pharmacology and function of GPR35 in the nervous system[J]. *Neuropharmacology*, 2017, 113: 661-671.
- [2] Taniguchi Y, Tonai-Kachi H, Shinjo K. Zaprinast, a well-known cyclic guanosine monophosphate-specific phosphodiesterase inhibitor, is an agonist for GPR35[J]. *FEBS letters*, 2006, 580(21): 5003-5008.
- [3] Halene T B, Siegel S J. PDE inhibitors in psychiatry—future options for dementia, depression and schizophrenia?[J]. *Drug discovery today*, 2007, 12(19-20): 870-878.
- [4] Gibson A. Phosphodiesterase 5 inhibitors and nitrgergic transmission—from zaprinast to sildenafil[J]. *European journal of pharmacology*, 2001, 411(1-2): 1-10.
- [5] Giorgi M, Leonetti C, Citro G, et al. In vitro and in vivo inhibition of SK-N-MC neuroblastoma growth using cyclic nucleotide phosphodiesterase inhibitors[J]. *Journal of neuro-oncology*, 2001, 51(1): 25-31.
- [6] Lee H S, Kwon S H, Ham J E, et al. Zaprinast activates MAPKs, NFκB, and Akt and induces the expressions of inflammatory genes in microglia[J]. *International immunopharmacology*, 2012, 13(3): 232-241.
- [7] Choi J H, Kim D H, Yun I J, et al. Zaprinast inhibits hydrogen peroxide-induced lysosomal destabilization and cell death in astrocytes[J]. *European journal of pharmacology*, 2007, 571(2-3): 106-115.
- [8] Pifarré P, Prado J, Giralt M, et al. Cyclic GMP phosphodiesterase inhibition alters the glial inflammatory response, reduces oxidative stress and cell death and increases angiogenesis following focal brain injury[J]. *Journal of neurochemistry*, 2010, 112(3): 807-817.
- [9] Hodges W T, Jarasvaraparn C, Ferguson D, et al. Mitochondrial pyruvate carrier inhibitors improve metabolic parameters in diet-induced obese mice[J]. *Journal of Biological Chemistry*, 2022, 298(2): 101554.

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