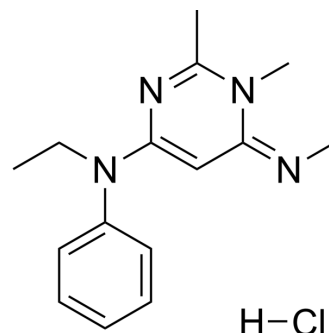


## ZD7288

|                    |  |
|--------------------|--|
| Cat. No.:          | HY-101346  |
| CAS No.:           | 133059-99-1  |
| Molecular Formula: | C <sub>15</sub> H <sub>21</sub> ClN <sub>4</sub>   |
| Molecular Weight:  | 292.81   |
| Target:            | HCN Channel  |
| Pathway:           | Membrane Transporter/Ion Channel   |
| Storage:           | 4°C, sealed storage, away from moisture<br>* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture) |



### SOLVENT & SOLUBILITY

| In Vitro  | DMSO : 50 mg/mL (170.76 mM; Need ultrasonic)   |                       |            |            |  |      |      |       |      |           |            |            |      |           |           |           |       |           |           |           |
|---|--|-----------------------|------------|------------|--|------|------|-------|------|-----------|------------|------------|------|-----------|-----------|-----------|-------|-----------|-----------|-----------|
|   | H <sub>2</sub> O : ≥ 50 mg/mL (170.76 mM)<br>* "≥" means soluble, but saturation unknown.  |                       |            |            |  |      |      |       |      |           |            |            |      |           |           |           |       |           |           |           |
| Preparing Stock Solutions   | <table border="1"> <thead> <tr> <th rowspan="2">Solvent Concentration</th> <th colspan="3">Mass</th> </tr> <tr> <th>1 mg</th> <th>5 mg</th> <th>10 mg</th> </tr> </thead> <tbody> <tr> <td>1 mM</td> <td>3.4152 mL</td> <td>17.0759 mL</td> <td>34.1518 mL</td> </tr> <tr> <td>5 mM</td> <td>0.6830 mL</td> <td>3.4152 mL</td> <td>6.8304 mL</td> </tr> <tr> <td>10 mM</td> <td>0.3415 mL</td> <td>1.7076 mL</td> <td>3.4152 mL</td> </tr> </tbody> </table> | Solvent Concentration | Mass       |            |  | 1 mg | 5 mg | 10 mg | 1 mM | 3.4152 mL | 17.0759 mL | 34.1518 mL | 5 mM | 0.6830 mL | 3.4152 mL | 6.8304 mL | 10 mM | 0.3415 mL | 1.7076 mL | 3.4152 mL |
|   | Solvent Concentration  |                       | Mass       |            |  |      |      |       |      |           |            |            |      |           |           |           |       |           |           |           |
|   |  | 1 mg                  | 5 mg       | 10 mg      |  |      |      |       |      |           |            |            |      |           |           |           |       |           |           |           |
|   | 1 mM   | 3.4152 mL             | 17.0759 mL | 34.1518 mL |  |      |      |       |      |           |            |            |      |           |           |           |       |           |           |           |
| 5 mM  | 0.6830 mL  | 3.4152 mL             | 6.8304 mL  |            |  |      |      |       |      |           |            |            |      |           |           |           |       |           |           |           |
| 10 mM   | 0.3415 mL  | 1.7076 mL             | 3.4152 mL  |            |  |      |      |       |      |           |            |            |      |           |           |           |       |           |           |           |
| Please refer to the solubility information to select the appropriate solvent. |  |                       |            |            |  |      |      |       |      |           |            |            |      |           |           |           |       |           |           |           |
| In Vivo   | 1. Add each solvent one by one: PBS<br>Solubility: 100 mg/mL (341.52 mM); Clear solution; Need ultrasonic  |                       |            |            |  |      |      |       |      |           |            |            |      |           |           |           |       |           |           |           |

### BIOLOGICAL ACTIVITY

|                           |   |
|---------------------------|---|
| Description               | ZD7288 (ICI D7288) is a selective hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blocker <sup>[1]</sup> .  |
| IC <sub>50</sub> & Target | HCN channel <sup>[1]</sup>  |
| In Vitro                  | ZD7288 is a selective hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blocker. ZD7288 inhibits glutamate release in a concentration-dependent manner. After incubation with 1, 5 and 50 μM ZD7288 for 24 hours, glutamate content in extracellular fluid is decreased to 69.0±2.8%, 31.4±2.0% and 4.4±0.3%, respectively (P<0.01, vs. DMEM/F12 group [100.2±4.2%]). After incubation with ZD7288 (25, 50, or 100 μM) for 20 minutes, 50 μM glutamate-induced [Ca <sup>2+</sup> ] <sub>i</sub> rises are attenuated to 59.2±2.7%, 41.4±2.3% and 21.0±1.4%, respectively glutamate (P<0.01, vs. 50 μM glutamate group) <sup>[1]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| In Vivo                   | Application of ZD7288 0.1 μM at 5 minutes before high-frequency stimulation significantly decreases the amplitude of field  |

excitatory postsynaptic potentials (fEPSPs), and this inhibitory effect is maintained throughout the recording period. Application of 0.1  $\mu$ M ZD7288 30 minutes after high-frequency stimulation almost completely reverses the established long-term potentiation (LTP). Following application of ZD7288 (0.1  $\mu$ M) 5 minutes before high-frequency stimulation, glutamate content is reduced to 74.9 $\pm$ 8.0% (P<0.05, vs. normal saline group). Furthermore, application of 0.1  $\mu$ M ZD7288 30 minutes after high-frequency stimulation markedly decreases the glutamate content to 77.0% $\pm$ 9.4% (P<0.05, vs. normal saline group)<sup>[1]</sup>.

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

## PROTOCOL

### Cell Assay <sup>[1]</sup>

Primary hippocampal neurons are obtained from neonatal (1 to 2 day-old) Sprague-Dawley rats, and used in this study. The cells are incubated for 24 hours with ZD7288 (1, 5, or 50  $\mu$ M), 8-bromoadenosine cyclic adenosine monophosphate (8-Br-cAMP, 5 or 50  $\mu$ M), or forskolin (1 or 5  $\mu$ M), and the culture medium is collected for glutamate measurement<sup>[1]</sup>.

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

### Animal Administration <sup>[1]</sup>

Specific-pathogen-free adult male Sprague-Dawley rats, aged 10 weeks and weighing 200 $\pm$ 20 g are used in this study. For hippocampal administration of saline or drugs, a cannula is carefully inserted into the CA3 area with an introductory tube fixed parallel to the recording electrode, reaching 0.1 to 0.2 mm higher than the electrode tip. To test the effects of blockers on the induction of long-term potentiation (LTP), 0.1  $\mu$ M ZD7288 or the monovalent cation cesium (Cs<sup>+</sup>) is applied 5 minutes before high-frequency stimulation. To test the effects of blockers on the maintenance of LTP, ZD7288/Cs<sup>+</sup> is slowly administered using an infusion/withdrawal pump 30 minutes after the high-frequency stimulation<sup>[1]</sup>.

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

## CUSTOMER VALIDATION

- J Headache Pain. 2023 Apr 21;24(1):44.
- J Affect Disorders. 2022 Dec 29;324:143-152.
- Neuropharmacology. 2020 Oct 1;176:108222.
- bioRxiv. 2023 Mar 5.
- Research Square Print. October 6th, 2022.

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## REFERENCES

[1]. Zhang XX, et al. ZD7288, a selective hyperpolarization-activated cyclic nucleotide-gated channel blocker, inhibits hippocampal synaptic plasticity. Neural Regen Res. 2016 May;11(5):779-86.

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

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