# Product Data Sheet

Product Name: LY 2389575 hydrochloride
Cat. No.: GC14722

## Chemical Properties

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|---|---|---|---|
| Cas. No. | 885104-09-6 | | |
| Chemical Name | (S)-1-(5-bromopyrimidin-2-yl)-N-(2,4-dichlorobenzyl)pyrrolidin-3-amine hydrochloride | | |
| SMILES | BrC1=CN=C(N2CC[C@@](NCC3=C(Cl)C=C(Cl)C=C3)([H])C2)N=C1.Cl | | |
| Formula | $C_{15}H_{15}BrCl_2N_4.HCl$ | M.Wt | 438.58 |
| Solubility | <8.77mg/ml in DMSO | Storage | Desiccate at RT |
| General tips | For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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 | LY 2389575 hydrochloride | | |

## Background

LY2389575 is described here instead of LY2389575 hydrochloride. LY2389575 is a selective negative allosteric modulator (NAM) of metabotropic glutamate receptor 3 (mGlu3) with an IC50 value of 4.2 μM [1].

The metabotropic glutamate receptors (mGlus) are members of the GPCR family C. They are characterized by a large extracellular amino-terminal domain for binding agonist. Eight mGlus had been found and were assigned to three groups based on their pharmacology, sequence homology, and mechanisms to couple to effector. They are Group I: mGlu1 and mGlu5; Group II: mGlu2 and mGlu3; Group III: mGlu4,6,7,8 [1].

In mixed neuronal cultures, LY2389575 abolished the protective activity of 1 μM LY379268 (the orthosteric mGlu2/3 receptor agonist) in the concentration range of 0.1 to 1 μM and amplified Aβ toxicity on its own at the highest concentration. In the absence of Aβ, LY2389575 at these concentrations was not toxic (numbers of dead neurons in control cultures and in cultures treated with 1 μM LY2389575 were 41 ± 3, and 42 ± 1,


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respectively). Further data indicated that LY2389575 was able to amplify Aβ toxicity and abolish the neuroprotective activity of LY379268 only in cultures containing wild-type astrocytes. In the FLIPR assay system, LY2389575 behaved as a noncompetitive mGlu3 receptor antagonist with an efficacy of 100 ± 0.68% and an IC50 value of 190 ± 26 nM. LY2389575 failed in affecting responses mediated by all other mGlu receptor subtypes or GABAB receptors [2].

No in vivo data for the application of this drug had been found.

References:
[1]. Sheffler DJ, Wenthur CJ, Bruner JA, et al. Development of a novel, CNS-penetrant, metabotropic glutamate receptor 3 (mGlu3) NAM probe (ML289) derived from a closely related mGlu5 PAM[J]. Bioorganic & medicinal chemistry letters, 2012, 22(12): 3921-3925.
[2]. Caraci F, Molinaro G, Battaglia G, et al. Targeting Group II Metabotropic Glutamate (mGlu) Receptors for the Treatment of Psychosis Associated with Alzheimer's Disease: Selective Activation of mGlu2 Receptors Amplifies β-Amyloid Toxicity in Cultured Neurons, Whereas Dual Activation of mGlu2 and mGlu3 Receptors Is Neuroprotective[J]. Molecular pharmacology, 2011, 79(3): 618-626.