Semagacestat  
Item No. 16713

CAS Registry No.: 425386-60-3
Formal Name: (2S)-2-hydroxy-3-methyl-N-[(1S)-1-methyl-2-oxo-2-[(1S)-2,3,4,5-tetrahydro-3-methyl-2-oxo-1H-3-benzazepin-1-yl]amino]ethyl]-butanamide
Synonym: LY450139
MF: C$_{19}$H$_{27}$N$_{3}$O$_{4}$
FW: 361.4
Purity: ≥98%
Stability: ≥2 years at -20°C
Supplied as: A crystalline solid

Laboratory Procedures
For long term storage, we suggest that semagacestat be stored as supplied at -20°C. It should be stable for at least two years. Semagacestat is supplied as a crystalline solid. A stock solution may be made by dissolving the semagacestat in the solvent of choice. Semagacestat is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of semagacestat in ethanol is approximately 1 mg/ml and approximately 25 mg/ml in DMSO and DMF.

Semagacestat is sparingly soluble in aqueous solutions. To enhance aqueous solubility, dilute the organic solvent solution into aqueous buffers or isotonic saline. If performing biological experiments, ensure the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. We do not recommend storing the aqueous solution for more than one day.

γ-Secretase is a protease complex that cleaves single-pass transmembrane proteins, such as Notch receptors and β-amyloid precursor protein (APP), within the transmembrane domain. Semagacestat is a potent inhibitor of γ-secretase that blocks the production of Aβ38, Aβ40, and Aβ42 with IC$_{50}$ values of 12.0, 12.1, and 10.9 nM, respectively. It also blocks Notch signaling (IC$_{50}$ = 14.1 nM). Semagacestat modulates γ-secretase activity in vivo, altering Aβ levels in brain, cerebrospinal fluids, and plasma in a dose-dependent fashion. Although semagacestat does not improve cognitive status in humans, it is useful as a pan γ-secretase inhibitor for research purposes.

References

Related Products
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