

Product Data Sheet

Product Name: AZ1136
Cat. No.: GC79793

Chemical Properties

Cas. No. 1380508-60-0

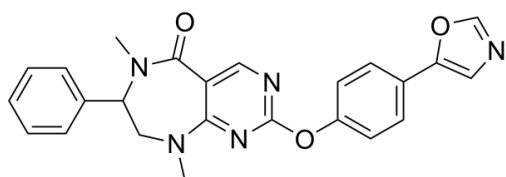
Formula $C_{24}H_{21}N_5O_3$ M.Wt 427.46

Solubility Storage Store at -20°C

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



Background

AZ1136 is a γ -secretase modulator that regulates amyloid- β ($A\beta$) production without reducing total $A\beta$ generation. AZ1136 also modulates γ -secretase-mediated Notch S4 cleavage, but does not inhibit NICD formation. AZ1136 can be used in studies related to γ -secretase, APP processing and Alzheimer's disease [1] [2] [3].

In Vitro, AZ1136 (25 μ M; 2 h) modulates γ -secretase-mediated APP processing in HEK/APPswe cell membranes, reduces the levels of $A\beta$ 42 and $A\beta$ 40, increases the levels of short-chain $A\beta$ 37 and $A\beta$ 38, alters specific short peptide cleavage products, and preferentially affects the turnover of $A\beta$ 42

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

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without inhibiting the overall activity of γ -secretase^[1]. AZ1136 modulates γ -secretase-mediated A β production in HEK/APPswe cells, potentially reduces the levels of amyloidogenic A β 42 (IC₅₀ = 990 nM) and A β 40 (IC₅₀ = 1400 nM), while increasing the shorter, less amyloidogenic A β 37 and A β 39, without altering total A β levels^[2]. AZ1136 (25 μ M; 16 h) reduces A β 40 and A β 42 by 2.3-fold and 8.3-fold, respectively, increases A β 37 and A β 39 by 3.5-fold and 2.1-fold, respectively, in HEK/APPswe cells, while A β 38 remains unaffected^[2]. AZ1136 (5 h) modulates γ -secretase-mediated APP processing in HEK/APPswe cells, reduces the levels of A β 42 (IC₅₀ 990 nM) and A β 40 (IC₅₀ 1400 nM) (with higher potency against A β 42), and increases the shorter A β 37 and A β 39 peptides, without altering total A β levels or inducing cytotoxicity^[3]. AZ1136 (0-5 μ M; 5 h) competes with AZ4800 for binding to a common molecular target in HEK/APPswe cells, indicating that both belong to the same class of second-generation γ -secretase modulators^[3]. AZ1136 (2 h) retains A β -modulating activity in both HEK/APPswe-derived total membranes (TM) and carbonate-extracted membranes (CEM), significantly inhibiting A β 42 and increasing A β 37; a slight increase in A β 38 is also observed in this cell-free membrane assay^[3]. AZ1136 (25 μ M; 24 h) modulates γ -secretase-mediated Notch N peptide production in HEK/FLAG-Notch1- Δ E cells, reducing F-N24 and F-N25 by 2.0-fold and 2.6-fold, respectively, and increasing F-N18 by 1.7-fold^[2].

References:

- [1]. Olsson F, et al. Characterization of intermediate steps in amyloid beta (A β) production under near-native conditions. The Journal of biological chemistry. 2014 Jan 17;289(3):1540-50.
- [2]. Wanngren J, et al. Second generation γ -secretase modulators exhibit different modulation of Notch β and A β production. The Journal of biological chemistry. 2012 Sep 21;287(39):32640-50.
- [3]. Borggaard T, et al. First and second generation γ -secretase modulators (GSMs) modulate amyloid- β (A β) peptide production through different mechanisms. The Journal of biological chemistry. 2012 Apr 06;287(15):11810-9.

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