Verubecestat TFA

Cat. No.: HY-16759A

CAS No.: 2095432-65-6

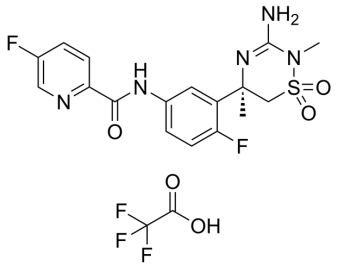
Molecular Formula: $C_{19}H_{18}F_5N_5O_5S$

Molecular Weight: 523.43

Target: Beta-secretase

Pathway: Neuronal Signaling

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Verubecestat (MK-8931) TFA is an orally active, high-affinity BACE1 and BACE2 inhibitor with K_i values of 2.2 nM and 0.38 nM. Verubecestat TFA effectively reduces Aβ40 and has the potential for Alzheimer's Disease[1][2].
IC_{50} & Target	Ki: 2.2 nM (BACE1) and 0.38 nM (BACE2)[1]
In Vitro	Verubecestat TFA (MK-8931) is a β-site amyloid precursor protein cleaving enzyme 1/2 (BACE1/2) inhibitor. Verubecestat TFA does not significantly inhibit human CYP isoforms 1A2, 2C9, 2C19, 2D6, and 3A4 (all IC_{50}>40 μM), indicating that the compound is unlikely to be a perpetrator of CYP-mediated drug-drug interactions[1]. Verubecestat TFA has IC_{50}s of 2.1 nM, 0.7 nM, 4.4 nM for Aβ1-40, Aβ1-42, sAPPβ in HEK293 $APP^{Swe/Lon}$ cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Verubecestat TFA (MK-8931; 3 mg/kg; IV or oral) has a $T_{1/2}$ of 1.9 hours, a CL of 46 mL/min/kg, a V_{ss} of 5.4 L/kg, a C_{max} of 0.27 μM and a AUC of 1.1 μM•h for Sprague-Dawley (SD) rats[1]. Verubecestat TFA (1 mg/kg; IV) has a $T_{1/2}$ of 4.9 hours, a CL of 21 mL/min/kg, a V_{ss} of 7.5 L/kg for cynomolgus monkeys[1]. Verubecestat TFA (1 mg/kg; IV) has a $T_{1/2}$ of 9.7 hours, a CL of 4.3 mL/min/kg, a V_{ss} of 2.7 L/kg for beagle dogs[1]. Verubecestat TFA (30 mg/kg; orally; BID for 5 days) causes a modest (1.4-fold) induction of CYP 3A1 activity but does not significantly alter the expression of CYPs 1A1, 1A2, 2B, 3A2, or 4A in rats[1]. Verubecestat TFA dose-dependently reduces CSF and cortex Aβ40 with ED_{50} values of 5 and 8 mg/kg, respectively, corresponding to unbound plasma EC_{50} values of 48 and 81 nM, respectively[1]. Verubecestat TFA (3 and 10 mg/kg; orally) reduces profound, sustained of CSF Aβ40 levels and has peak effects on CSF Aβ lowering (72 and 81% reduction at 3 and 10 mg/kg, respectively) 12 h after dosing[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Differ. 2022 Jun 22.
- Microorganisms. 2023 Jun 18, 11(6), 1608.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Yan R, et al. Stepping closer to treating Alzheimer's disease patients with BACE1 inhibitor drugs. Transl Neurodegener. 2016 Jul 14;5:13.

[2]. Scott JD, et al. Discovery of the 3-Imino-1,2,4-thiadiazinane 1,1-Dioxide Derivative Verubecestat (MK-8931)-A β-Site Amyloid Precursor Protein Cleaving Enzyme 1 Inhibitor for the Treatment of Alzheimer'sDisease. Med Chem. 2016 Dec 8;59(23):10435-10450.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA