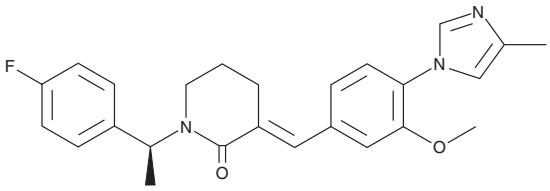
PRODUCT INFORMATION

E2012

Item No. 29710

CAS Registry No.:	870843-42-8
Formal Name:	(3E)-1-[(1S)-1-(4-fluorophenyl) ethyl]-3-[[3-methoxy-4-(4-methyl-1H-imidazol-1-yl)phenyl] methylene]-2-piperidinone
MF:	$C_{25}H_{26}FN_3O_2$
FW:	419.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 286 nm
Supplied as:	A solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

E2012 is supplied as a solid. A stock solution may be made by dissolving the E2012 in the solvent of choice, which should be purged with an inert gas. E2012 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of E2012 in these solvents is approximately 10 mg/ml.

E2012 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, E2012 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. E2012 has a solubility of approximately 0.25 mg/ml in a 1:3 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

E2012 is a modulator of γ-secretase.[1] It selectively inhibits APP intracellular signaling domain (AICD) cleavage to amyloid-β (Aβ) over Notch cleavage to its signaling effector Notch intracellular domain (NICD), processes both mediated by γ-secretase, when used at a concentration of 1 µM in luciferase assays.[2] E2012 also inhibits the activity of the cholesterol synthesis enzyme 3β-hydroxysterol Δ^{24}-reductase (DHCR24) in primary rat hepatocytes and HepG2 cells (IC_{50}s = 11 and 15 nM, respectively).[3] It reduces Aβ (1-42) (Aβ42) production in primary rat embryonic cerebral cortex neurons with an IC_{50} value of 220 nM.[4] E2012 (100 mg/kg) also decreases Aβ42 levels in guinea pig brain and cerebral spinal fluid (CSF).[5]

References

1. Hahn, S., Brüning, T., Ness, J., *et al.* Presenilin-1 but not amyloid precursor protein mutations present in mouse models of Alzheimer's disease attenuate the response of cultured cells to γ-secretase modulators regardless of their potency and structure. *J. Neurochem.* **116(3)**, 385-395 (2011).
2. Dimitrov, M., Alattia, J.-R., Lemmin, T., *et al.* Alzheimer's disease mutations in APP but not γ-secretase modulators affect epsilon-cleavage-dependent AICD production. *Nat. Commun.* **4:2246** (2013).
3. Nakano-Ito, K., Fujikawa, Y., Hihara, T., *et al.* E2012-induced cataract and its predictive biomarkers. *Toxicol. Sci.* **137(1)**, 249-258 (2014).
4. Kimura, T., Kawano, K., Doi, E., *et al.* Cinnamide compound. *Eisai Co., Ltd.* **WO2005/115990A1** (2005).
5. Lu, Y., Riddell, D.R., Hajos-Korcsok, E., *et al.* Cerebrospinal fluid amyloid-β (Aβ) as an effect biomarker for brain Aβ lowering verified by quantitative preclinical analyses. *J. Pharmacol. Exp. Ther.* **342(2)**, 366-375 (2012).

CAYMAN CHEMICAL
1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA
PHONE: [800] 364-9897
[734] 971-3335
FAX: [734] 971-3640
CUSTSERV@CAYMANCHEM.COM
WWW.**CAYMANCHEM**.COM