

Product Specification Sheet

Product Name: BMS-708163 (Avagacestat)

Catalog Number: C2708

Technical information:

Chemical Formula: $C_{20}H_{17}ClF_4N_4O_4S$

CAS #: 1146699-66-2

Molecular Weight: 520.88

Purity: > 98%

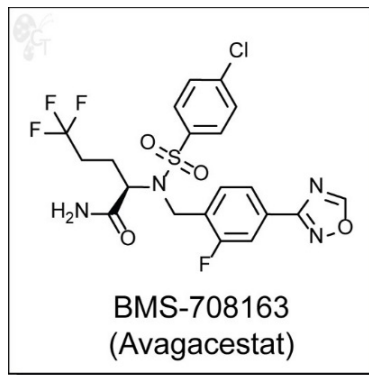
Appearance: White

Solubility: Soluble in DMSO up to 50 mM

Chemical Name: (2R)-2-(N-(2-fluoro-4-(1,2,4-oxadiazol-3-yl)benzyl)-4-chlorophenylsulfonamido)-5,5,5-trifluoropentanamide

Storage: Store solid powder at 4°C desiccated; Store DMSO solution at -20°C.

Shelf Life: In the unopened package, powder is stable for 1 year and DMSO solution is stable for 6 months under proper storage condition.



- Handling:**
- To make 10 mM stock solution, add 0.192mL of DMSO for each mg of BMS-708163 (Avagacestat)
 - For DMSO solution, briefly spin the vial at 500 rpm in a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity: BMS-708163 (Avagacestat) is a potent and selective inhibitor for γ -secretase, especially at inhibiting cleavage of amyloid precursor protein (APP) to form amyloid- β ($A\beta$)(1-40) (IC_{50} =0.3nM) and $A\beta$ (1-42) (0.27nM). BMS-708163 is “Notch sparing”, with more than 100 folds more selective for APP than for Notch protein (IC_{50} of 58nM).

BMS-708163 is developed for treating Alzheimer’s disease (AD). Oral administration of BMS-708163 significantly reduced $A\beta$ (1-40) levels for sustained periods in brain, plasma, and cerebrospinal fluid in rats and dogs [1]. The results of Phase II clinical trial in mild-to-moderate AD patients demonstrated acceptable tolerability at a single-dose range of 0.3 to 800 mg with a biphasic effect on plasma $A\beta$ (1-40) [2].

- Reference:**
1. Gillman, KW., et al. Discovery and Evaluation of BMS-708163, a Potent, Selective and Orally Bioavailable γ -Secretase Inhibitor. ACS Med. Chem. Lett., 2010, 1 (3): 120–124 Pubmed ID:
 2. Tong G., et al., Multicenter, randomized, double-blind, placebo-controlled, single-ascending dose study of the oral γ -secretase inhibitor BMS-708163 (Avagacestat): tolerability profile, pharmacokinetic parameters, and pharmacodynamic markers. Clin Ther. 2012 . 34(3):654-67. Pubmed ID: 22381714

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