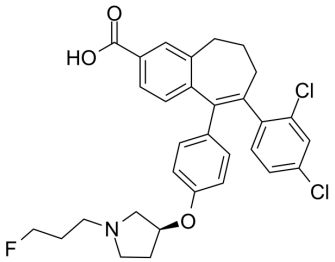
Amcenestrant

Cat. No.:	HY-133017
CAS No.:	2114339-57-8
Molecular Formula:	$C_{31}H_{30}Cl_2FNO_3$
Molecular Weight:	554.48
Target:	Estrogen Receptor/ERR
Pathway:	Vitamin D Related/Nuclear Receptor
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 83.33 mg/mL (150.28 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8035 mL	9.0175 mL	18.0349 mL
	5 mM	0.3607 mL	1.8035 mL	3.6070 mL
	10 mM	0.1803 mL	0.9017 mL	1.8035 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 8.33 mg/mL (15.02 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 8.33 mg/mL (15.02 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 8.33 mg/mL (15.02 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SAR439859 (compound 43d) is an orally active, nonsteroidal and selective estrogen receptor degrader (SERD). SAR439859 is a potent ER antagonist and has ER degrading activity with an EC_{50} of 0.2 nM for ERα degradation[1]. SAR439859 demonstrates robust antitumor efficacy and limited cross-resistance in ER^+ breast cancer[2].

IC_{50} & Target

ERα
0.2 nM (EC50)

In Vitro

SAR439859 (compound 43d) induces strong in vivo antitumor activity against a variety of BC cell lines and patient-derived xenografts, including models that harbor ERα mutations[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

SAR439859 (compound 43d; orally; 2.5-25 mg/kg; twice daily for 30 days) exhibits substantial tumor-growth inhibition and displays tumor regression at the dose of 25 mg/kg/BID[1].

SAR439859 (3 mg/kg for iv and 10 mg/kg for po) shows a low to moderate clearance in the three animal species tested (0.03-1.92 L/h•kg), low to moderate volume of distribution (V_{ss}=0.5-6.1 L/kg), and good bioavailability (54-76%) across species. It is noticed that $T_{1/2}$ was variable across species (1.98 h in mouse, 4.13 h in rat and 9.80 h in dog)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Nu/nu mouse with MCF7 tumor xenograft model[1]
Dosage:	2.5, 5, 12.5, 25 mg/kg
Administration:	Orally; twice daily for 30 days
Result:	Exhibited substantial tumor-growth inhibition and displayed tumor regression at the dose of 25 mg/kg/BID.

Animal Model:	Mouse, rat and dog[1]
Dosage:	3 mg/kg (iv) and 10 mg/kg (po) (Pharmacokinetic Analysis)
Administration:	Iv or po
Result:	Showed a low to moderate clearance in the three animal species tested (0.03-1.92 L/h•kg), low to moderate volume of distribution (V_{ss}=0.5-6.1 L/kg), and good bioavailability (54-76%) across species.

REFERENCES

[1]. El-Ahmad Y, et al. Discovery of 6-(2,4-Dichlorophenyl)-5-[4-[(3S)-1-(3-fluoropropyl)pyrrolidin-3-yl]oxyphenyl]-8,9-dihydro-7H-benzo[7]annulene-2-carboxylic acid (SAR439859), a Potent and Selective Estrogen Receptor Degrader (SERD) for the Treatment of Est

[2]. Monsif Bouaboula, et al. Abstract 943: SAR439859, an orally bioavailable selective estrogen receptor degrader (SERD) that demonstrates robust antitumor efficacy and limited cross-resistance in ER^+ breast cancer.

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