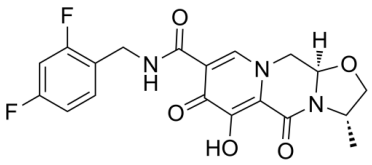
Data Sheet

Product Name:	Cabotegravir
Cat. No.:	CS-5078
CAS No.:	1051375-10-0
Molecular Formula:	$C_{19}H_{17}F_2N_3O_5$
Molecular Weight:	405.35
Target:	HIV; HIV Integrase; OAT
Pathway:	Anti-infection; Membrane Transporter/Ion Channel; Metabolic Enzyme/Protease
Solubility:	DMSO : 16.67 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

Cabotegravir (GSK-1265744) is a orally active and long-acting **HIV integrase** strand transfer inhibitor and organic anion transporter 1/3 (**OAT1**/**OAT3**) inhibitor with **IC_{50}** values of 2.5 nM, 0.41 μM and 0.81 μM for HIV_{ADA}, OAT3 and OAT1, respectively. Cabotegravir is primarily metabolized by uridine diphosphate glucuronosyltransferase (UGT) 1A1, with low potential to interact with other antiretroviral drugs (ARVs). Cabotegravir can be used to research AIDS[1][2]. IC50 & Target:IC_{50}: 2.5 nM (HIV_{ADA})[1]
IC_{50}: 0.41 μM (OAT3), 0.81 μM (OAT1)[2] ***In Vitro:*** Cabotegravir (GSK-1265744) inhibits the HIV-1 integrase catalyzed strand transfer reaction with an IC_{50} of 3.0 nM in vitro. The antiviral EC_{50} against HIV-1 Ba-L is 0.22 nM and that against NL432 is 0.34 nM in PBMCs, 0.57 nM using CellTiter-Glo and 1.3 nM using MTT in MT-4, and 0.5 nM in the PHIV assay, which uses a pseudotyped self-inactivating virus[3]. ***In Vivo:*** The half-life of Cabotegravir is up to 54 days in mice[1].
Cabotegravir (25 or 50 mg/kg; i.v.; single dose or twice) protects Macaques against intravenous challenge with SIVmac251[4].

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay [1] The inhibitory effect of CAB on bile salt export pump (BSEP), multidrug resistance-associated protein (MRP) 2 and MRP4 is investigated using membrane vesicles prepared from recombinant baculovirus-infected Sf9 cells expressing human BSEP, MRP2 or MRP4. The BSEP and MRP probe substrates, [3H]taurocholic acid (TC) and [3H]EG, respectively, and vesicle reagent kits are obtained commercially from GenoMembrane. The inhibition assays are performed using the conditions recommended by GenoMembrane. Briefly, vesicles (25-50 μg protein) are preincubated for 5-10 min at 37°C in reaction buffer with CAB (0.03-30 μM) or positive control inhibitor, benzbromarone (MRP2; 0.1-100 μM), indomethacin (MRP4; 0.3-150 μM) or rifampicin (BSEP; 0.1-100 μ M). Reactions are initiated by the addition of MgATP solution containing probe substrate: 50 μM [3H]EG (MRP2), 10 μM [3H]EG (MRP4), or 2 μM [3H]TC (BSEP). Additional incubations are performed in the absence of inhibitor and in the presence of MgAMP solution for passive transport. After 2-5 minutes, reactions are terminated by the addition of chilled stopping buffer and samples transferred to 96-well glass fiber filter plates, washed and radioactivity measured using LSC.

References:

[1]. Reese MJ, et al. Drug interaction profile of the HIV integrase inhibitor cabotegravir: assessment from in vitro studies and a clinical investigation with midazolam. Xenobiotica. 2015 Sep 4:1-12.

[2]. Zhou T, et al. Creation of a nanoformulated cabotegravir prodrug with improved antiretroviral profiles. Biomaterials. 2018 Jan;151:53-65.

[3]. Yoshinaga T, et al. Antiviral characteristics of GSK1265744, an HIV integrase inhibitor dosed orally or by long-acting injection. Antimicrob Agents Chemother. 2015 Jan;59(1):397-406.

[4]. Andrews CD, et al. Cabotegravir long acting injection protects macaques against intravenous challenge with SIVmac251. AIDS. 2017 Feb 20;31(4):461-467.

CAIndexNames:

Oxazolo[3,2-a]pyrido[1,2-d]pyrazine-8-carboxamide, N-[(2,4-difluorophenyl)methyl]-2,3,5,7,11,11a-hexahydro-6-hydroxy-3-methyl-5,7-dioxo-, (3S,11aR)-

SMILES:

FC1=C(CNC(C2=CN3C(C(N([C@@H](C)CO4)[C@@]4([H])C3)=O)=C(O)C2=O)=O)C=CC(F)=C1

Tel: 610-426-3128 Fax: 888-484-5008 E-mail: sales@ChemScene.com

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