Ivacaftor-d4

Cat. No.: HY-13017S3

Molecular Formula: $C_{24}H_{24}D_4N_2O_3$

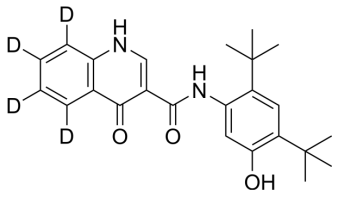
Molecular Weight: 396.52

Target: CFTR

Pathway: Membrane Transporter/Ion Channel

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



BIOLOGICAL ACTIVITY

Description	Ivacaftor-d4 (VX-770-d4) is the deuterium labeled-Ivacaftor (HY-13017). Ivacaftor is a potent and orally active CFTR potentiator, targeting G551D-CFTR and F508del-CFTR with EC_{50}s of 100 nM and 25 nM, respectively[1].
In Vitro	Ivacaftor (10 μM) increases the PC secretion activity by 3-fold for ABCB4-G535D, 13.7-fold for ABCB4-G536R, 6.7-fold for ABCB4-S1076C, 9.4-fold for ABCB4-S1176L, and 5.7-fold for ABCB4-G1178S. Ivacaftor corrects the functional defect of ABCB4 mutants[1]. Ivacaftor (10 μM) significantly increases CFTR activity in W1282X-expressing cells compared to R1162X CFTR cells[2]. Ivacaftor shows no significant activity against 160 targets tested including the $GABA_A$ benzodiazepine receptor. Ivacaftor increases the chloride secretion with an EC_{50} value of 0.236 ± 0.200 μM, a 10-fold shift in potency compared to the F508del HBEs[3]. In recombinant cells, Ivacaftor increases CFTR channel open probability (Po) in both the F508del processing mutation and the G551D gating mutation. Ivacaftor increases forskolin-stimulated I_T in temperature-corrected F508del-FRT cells by appr 6-fold with an EC_{50} of 25 nM[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Ivacaftor (1-200 mg/kg, p.o.) exhibits good oral bioavailability in rat[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Delaunay JL, et al. Functional defect of variants in the adenosine triphosphate-binding sites of ABCB4 and their rescue by the cystic fibrosis transmembrane conductance regulator potentiator, ivacaftor (VX-770). Hepatology. 2017 Feb;65(2):560-570

[2]. Mutyam V, et al. Therapeutic benefit observed with the CFTR potentiator, ivacaftor, in a CF patient homozygous for the W1282X CFTR nonsense mutation. J Cyst Fibros. 2017 Jan;16(1):24-29

[3]. Hadida S, et al. Discovery of N-(2,4-di-tert-butyl-5-hydroxyphenyl)-4-oxo-1,4-dihydroquinoline-3-carboxamide (VX-770, ivacaftor), a potent and orally bioavailable CFTR potentiator. J Med Chem. 2014 Dec 11;57(23):9776-9

[4]. Van Goor F, et al. Rescue of CF airway epithelial cell function in vitro by a CFTR potentiator, VX-770. Proc Natl Acad Sci U S A. 2009 Nov 3;106(44):18825-30.

Caution: Product has not been fully validated for medical applications. For research use only.

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