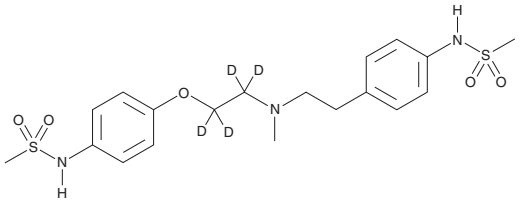
PRODUCT INFORMATION

Dofetilide-d_4

Item No. 26451

CAS Registry No.:	1189700-56-8
Formal Name:	N-[4-[2-[methyl[2-[4-[(methylsulfonyl) amino]phenoxy]ethyl-1,1,2,2-d_4]amino] ethyl]phenyl]-methanesulfonamide
MF:	$C_{19}H_{23}D_4N_3O_5S_2$
FW:	445.6
Chemical Purity:	≥98% (Dofetilide)
Deuterium Incorporation:	≥99% deuterated forms (d_1-d_4); ≤1% d_0
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

Dofetilide-d_4 is intended for use as an internal standard for the quantification of dofetilide (Item No. 15045) by GC- or LC-MS. The accuracy of the sample weight in this vial is between 5% over and 2% under the amount shown on the vial. If better precision is required, the deuterated standard should be quantitated against a more precisely weighed unlabeled standard by constructing a standard curve of peak intensity ratios (deuterated *versus* unlabeled).

Dofetilide-d_4 is supplied as a solid. A stock solution may be made by dissolving the dofetilide-d_4 in the solvent of choice, which should be purged with an inert gas. Dofetilide-d_4 is slightly soluble in chloroform and methanol.

Description

Dofetilide is a class III antiarrhythmic agent that prolongs cardiac action potential duration by selectively inhibiting the rapidly activating inward rectifying component of net delayed rectifier K^+ current (IC_{50} = 31.5 nM in guinea pig cardiomyocytes).[1] However, at 1 µM, dofetilide has pro-arrhythmic activity, inducing early afterdepolarizations (prolonged repolarization) in cell models and Torsade de Pointes in a rabbit screen for proarrhythmic properties when administered at a dose of 10 mg/kg.[2] Formulations containing dofetilide have been used in the treatment of highly symptomatic atrial fibrillation and the conversion of flutter to normal sinus rhythm.[3]

References

1. Jurkiewicz, N.K. and Sanguinetti, M.C. Rate-dependent prolongation of cardiac action potentials by a methanesulfonanilide class III antiarrhythmic agent. *Circ. Res.* **72(1)**, 75-83 (1993).
2. Nalos, L., Varkevisser, R., Jonsson, M.K., *et al.* Comparison of the I_{Kr} blockers moxifloxacin, dofetilide and E-4031 in five screening models of pro-arrhythmia reveals lack of specificity of isolated cardiomyocytes. *Br. J. Pharmacol.* **165(2)**, 467-478 (2012).
3. Dunnink, A., van Opstal, J.M., Oosterhoff, P., *et al.* Ventricular remodelling is a prerequisite for the induction of dofetilide-induced torsade de pointes arrhythmias in the anaesthetized, complete atrio-ventricular-block dog. *Europace* **14(3)**, 431-436 (2012).

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