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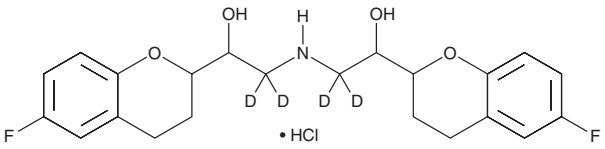
PRODUCT INFORMATION

(±)-Nebivolol-d_4 (hydrochloride)

Item No. 26659

Formal Name: 2,2'-azanediylbis(1-(6-fluorochroman-2-yl) ethan-2,2-d_2-1-ol), monohydrochloride
MF: $C_{22}H_{21}D_4F_2NO_4$ • HCl
FW: 445.9
Chemical Purity: ≥98% (mixture of diastereomers; Nebivolol)
Deuterium Incorporation: ≥99% deuterated forms (d_1-d_4); ≤1% d_0
Supplied as: A solid
Storage: -20°C
Stability: ≥2 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

(±)-Nebivolol-d_4 (hydrochloride) is intended for use as an internal standard for the quantification of nebivolol (Item No. 23660) 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).

(±)-Nebivolol-d_4 (hydrochloride) is supplied as a solid. A stock solution may be made by dissolving the (±)-nebivolol-d_4 (hydrochloride) in the solvent of choice. (±)-Nebivolol-d_4 (hydrochloride) is soluble in the organic solvent DMSO, which should be purged with an inert gas.

Description

Nebivolol is a potent and selective β_1-adrenergic receptor (β_1-AR) antagonist (IC_{50}s = 7.41 and 251 nM for β_1- and β_2-ARs, respectively, in a radioligand binding assay using rabbit lung membrane preparations).[1] It is also selective for β_1-ARs over serotonin 5-HT_{1A} and 5-HT_2, α_1- and α_2-adrenergic, histamine H_1, and dopamine D_2 receptors (IC_{50}s = 27.5 and 2,239, 3,162 and >10,000, 5,623, and 10,000 nM, respectively). Nebivolol inhibits cAMP accumulation induced by norepinephrine (Item No. 16673) in primary rat cardiac cells (IC_{50} = 22 nM) and induces vasodilation in mouse renal arteries *via* a nitric oxide- and cGMP-dependent mechanism (EC_{50} = 11.36 µM).[2,3] It decreases contraction of isolated human left ventricular trabeculae induced by isoproterenol (Item No. 15592; IC_{50} = 7.0 µM) but does not exert intrinsic sympathomimetic activity (ISA).[4] Nebivolol inhibits proliferation of human coronary artery smooth muscle cells (HCASMCs) in the presence and absence of growth factors (IC_{50}s = 6.1, 6.8, 6.4, and 7.7 µM for HCASMCs grown in media containing no growth factor, PDGFBB, basic FGF, and TGF-β1, respectively).[5] Formulations containing nebivolol have been used to treat hypertension.

References

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2. Pauwels, P.J., Leysen, J.E., and Janssen, P.A. *Eur. J. Pharmacol.* **172(6)**, 471-479 (1989).
3. Georgescu, A., Pluteanu, F., Flonta, M.L., *et al. Pharmacology* **81(2)**, 110-117 (2008).
4. Brixius, K., Bundkirchen, A., Bölck, B., *et al. Br. J. Pharmacol.* **133(8)**, 1330-1338 (2001).
5. Brehm, B.R., Wolf, S.C., Bertsch, D., *et al. Cardiovasc. Res.* **49(2)**, 430-439 (2001).

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