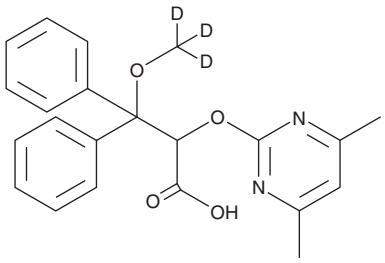
PRODUCT INFORMATION

Ambrisentan-d_3

Item No. 35558

CAS Registry No.:	1189479-60-4
Formal Name:	2-((4,6-dimethylpyrimidin-2-yl)oxy)-3-(methoxy-d_3)-3,3-diphenylpropanoic acid
MF:	$C_{22}H_{19}D_3N_2O_4$
FW:	381.4
Chemical Purity:	≥98% (Ambrisentan)
Deuterium Incorporation:	≥99% deuterated forms (d_1-d_3); ≤1% d_0
Supplied as:	A crystalline 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

Ambrisentan-d_3 is intended for use as an internal standard for the quantification of ambrisentan (Item No. 23669) 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).

Ambrisentan-d_3 is supplied as a crystalline solid. A stock solution may be made by dissolving the ambrisentan-d_3 in the solvent of choice, which should be purged with an inert gas. Ambrisentan-d_3 is soluble in the organic solvent DMSO.

Description

Ambrisentan is a nonpeptide endothelin A (ETA) receptor antagonist (IC_{50}s = 0.251, 0.316, 0.398, 251, and 630 nM for rat preparations of heart, bladder, kidney, lung, and cerebral cortex, respectively).[1] It inhibits contraction of isolated rabbit aortic rings induced by endothelin-1 (ET-1; Item No. 24127) by 43.23% when used at a concentration of 1 µM.[2] Ambrisentan inhibits ET-1-induced contraction of human pulmonary and radial arteries *in vitro* (K_d = 0.042 and 0.11 µM, respectively).[3] In a rat model of neonatal hyperoxic lung injury, ambrisentan (20 mg/kg per day, s.c.) reduces pulmonary arterial hypertension (PAH) as well as decreases PAH-induced right ventricular hypertrophy (RVH) and peak RV pressure.[4] Formulations containing ambrisentan have been used in the treatment of PAH.

References

1. Yokoyama, Y., Osano, A., Hyashi, H., *et al.* Endothelin-1 receptors in rat tissues: Characterization by bosentan, ambrisentan and CI-1020. *Biol. Pharm. Bull.* **37(3)**, 461-465 (2014).
2. Xia, J., Song, J., Zhen, L., *et al.* Synthesis and *in vitro* evaluation of ambrisentan analogues as potential endothelin receptor antagonists. *Bioorg. Med. Chem. Lett.* **21(13)**, 3894-3897 (2011).
3. Angus, J.A., Soeding, P.F., Hughes, R.J.A., *et al.* Functional estimation of endothelin-1 receptor antagonism by bosentan, macitentan and ambrisentan in human pulmonary and radial arteries *in vitro*. *Eur. J. Pharmacol.* **804**, 111-116 (2017).
4. Wagenaar, G.T., Laghmani, e.H., de Visser, Y.P., *et al.* Ambrisentan reduces pulmonary arterial hypertension but does not stimulate alveolar and vascular development in neonatal rats with hyperoxic lung injury. *Am. J. Physiol. Lung Cell Mol. Physiol.* **304(4)**, L264-L275 (2013).

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