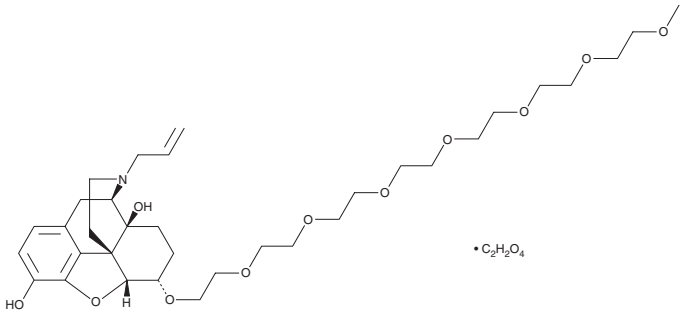
PRODUCT INFORMATION

Naloxegol (oxalate)

Item No. 23731

CAS Registry No.:	1354744-91-4
Formal Name:	(5α,6α)-4,5-epoxy-6-(3,6,9,12,15,18,21-heptaoxadocos-1-yloxy)-17-(2-propen-1-yl)-morphinan-3,14-diol, monoethanedioate
Synonyms:	AZ 13337019, NKTR-118
MF:	$C_{34}H_{53}NO_{11} \bullet C_2H_2O_4$
FW:	741.8
Purity:	≥98%
UV/Vis.:	λ_{max}: 212 nm
Supplied as:	A crystalline 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

Naloxegol (oxalate) is supplied as a crystalline solid. A stock solution may be made by dissolving the naloxegol (oxalate) in the solvent of choice, which should be purged with an inert gas. Naloxegol (oxalate) is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of naloxegol (oxalate) in these solvents is approximately 33, 20, and 16 mg/ml, respectively.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of naloxegol (oxalate) can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of naloxegol (oxalate) in PBS, pH 7.2, is approximately 10 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Description

Naloxegol is a peripherally acting antagonist of the μ-opioid receptor (K_i = 7.42 nM; pA_2 = 7.95).[1] It is selective for the μ-opioid receptor over the δ-opioid receptor (K_i = 866 nM). Naloxegol also acts as a partial agonist of κ-opioid receptors *in vitro* (EC_{50} = 47 nM for [^{35}S]GTPγS binding) but lacks activity *ex vivo* at concentrations up to 10 μM. *In vivo*, naloxegol reverses morphine-induced decreases in gastrointestinal motility and analgesia in a hot-plate assay in rats (ED_{50}s = 23.1 and 55.4 mg/kg, respectively), demonstrating a two-fold separation for peripheral *versus* CNS effects. Naloxegol also exhibits a brain uptake rate comparable to atenolol, a low-permeation standard with no brain uptake, in a rat brain perfusion model.

Reference

1. Floettmann, E., Bui, K., Sostek, M., *et al.* Pharmacologic profile of naloxegol, a peripherally acting μ-opioid receptor antagonist, for the treatment of opioid-induced constipation. *J. Pharmacol. Exp. Ther.* **361(2)**, 280-291 (2017).

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