

Catalog #10-4544 7-CI-O-Nec-1

CAS# 852391-15-2

 $5\hbox{-}((7\hbox{-}Chloro\hbox{-}1H\hbox{-}indol\hbox{-}3\hbox{-}yl)methyl)\hbox{-}3\hbox{-}methylimidazolidine\hbox{-}2,}4\hbox{-}dione; \hbox{\bf Nec-1s}$

Lot # FBA7194

Necrostatin-1 analogue with superior potency (IC $_{50}$ = 206nM vs 494nM), selectivity and metabolic stability in blocking RIP1. 1,2 7-Cl-O-Nec-1 shows no off-target inhibition of indolamine-2,3-deoxygenase (IDO) in contrast to Necrostatin-1 (Nec-1). 3,4 7-Cl-O-Nec-1 showed higher activity in inhibiting necroptosis in Jurkat cells than Necrostatin-1 (EC $_{50}$ = 210 nM vs. EC $_{50}$ = 490 nM), no non-specific cytotoxicity at high concentrations (100 μ M) and reasonable pharmacokinetic characteristics when used in mice. 2 7-Cl-O-Nec-1 is recommended for cellular and *in vivo* use over Necrostatin-1. 5

- 1) Degterev et al. (2005) Chemical inhibitor of nonapoptotic cell death with therapeutic potential for ischemic brain injury Nat.Chem.Biol. 1 112
- 2) Teng et al. (2005) Structure-activity relationship of novel necroptosis inhibitors Bioorg.Med.Chem.Lett. 15 5039
- 3) Degterev et al. (2012) Activity and specificity of necrostatin-1, small-molecule inhibitor of RIP1 kinase Cell Death Differ. **20** 366
- 4) Takahashi et al. (2012) Necrostatin-1 analogues: critical issues on the specificity, activity and in vivo use in experimental disease models Cell Death Dis. **3** e437
- 5) Degterev et al. (2013) Addendum: Chemical inhibitor of nonapoptotic cell death with therapeutic potential for ischemic brain injury Nat.Chem.Biol. **9** 192

PHYSICAL DATA

Molecular Weight: 277.71

Molecular Formula: C₁₃H₁₂ClN₃O₂

Purity: >98% by TLC (5% Methanol/methylene chloride: Rf = 0.55) and HPLC (Poroshell 120 C₁₈: 80%

CH₃CN + 0.05% TFA/ 20% H₂O + 0.05% TFA)

NMR: (Conforms)

Solubility: DMSO (>25 mg/ml)
Physical Description: Off-white to white

Storage and Stability: Store as supplied at -20°C for up to 1 year from the date of purchase. Solutions in

DMSO may be stored at -20°C for up to 3 months.