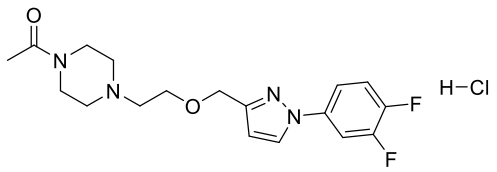
Product data sheet

MedKoo Cat#: 555898 Name: EST64454 HCl CAS#: 1950569-11-5 (HCl) Chemical Formula: $C_{18}H_{23}ClF_2N_4O_2$ Molecular Weight: 400.8548	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
EST64454 is a Highly Soluble σ1 Receptor Antagonist Clinical Candidate for Pain Management. EST64454 shows an outstanding aqueous solubility, which together with its high permeability in Caco-2 cells will allow its classification as a BCS class I compound.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	100.0	249.47

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.49 mL	12.47 mL	24.95 mL
5 mM	0.50 mL	2.49 mL	4.99 mL
10 mM	0.25 mL	1.25 mL	2.49 mL
50 mM	0.05 mL	0.25 mL	0.50 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Yeste S, Reinoso RF, Ayet E, Pretel MJ, Balada A, Serafini MT. Preliminary in Vitro Assessment of the Potential of EST64454, a Sigma-1 Receptor Antagonist, for Pharmacokinetic Drug-Drug Interactions. Biol Pharm Bull. 2020;43(1):68-76. doi: 10.1248/bpb.b19-00542. PMID: 31902934.

In vivo study

1. Díaz JL, García M, Torrens A, Caamaño AM, Enjo J, Sicre C, Lorente A, Port A, Montero A, Yeste S, Álvarez I, Martín M, Maldonado R, de la Puente B, Vidal-Torres A, Cendán CM, Vela JM, Almansa C. EST64454: a Highly Soluble σ1 Receptor Antagonist Clinical Candidate for Pain Management. J Med Chem. 2020 Dec 10;63(23):14979-14988. doi: 10.1021/acs.jmedchem.0c01575. Epub 2020 Nov 25. PMID: 33237785.

7. Bioactivity
Biological target:

EST64454 hydrochloride is a selective and orally active sigma-1 receptor antagonist with a Ki of 22 nM.

Product data sheet

In vitro activity

EST64454 is a selective sigma-1 receptor ligand intended for orally administered pain treatment that showed a promising profile in the lead optimization process. As part of the preliminary compound profiling, the potential for future drug-drug interactions was explored in vitro. Both direct and time-dependent CYP inhibition for CYP1A2, 2C9, 2C19, 2D6 and 3A4 was studied in human liver microsomes. EST64454 showed a low potential for CYP inhibition (IC50 between 100 and 1000 µM) and as time-dependent inhibitor (IC50 shift mainly around 1). CYP induction studies with HepaRG™ cells revealed no CYP induction at concentrations ⩽50 µM, as shown by the CYP1A2, 3A4 and 2B6 activities measured. EST64454 was not a P-glycoprotein (P-gp) substrate and was highly permeable in Caco-2 cells.

Reference: Biol Pharm Bull. 2020;43(1):68-76. https://pubmed.ncbi.nlm.nih.gov/31902934/

In vivo activity

The compound 9k (EST64454) showed in vivo efficacy after oral administration in two different pain models in mice: intraplantar capsaicin-induced mechanical hypersensitivity and partial sciatic nerve ligation (PSNL)-induced mechanical hypersensitivity, a model representative of neuropathic pain. In the capsaicin test, the antiallodynic potency of 9k was similar to that of the compound 1 (ED50 33 vs 28 mg/kg, respectively, Figure 3, Table 2). In the PSNL model, oral administration of 9k at 80 mg/kg, revealed an increased antiallodynic efficacy when comparing with the same dose of the compound 1 (95% vs 54%, respectively).

Reference: J Med Chem. 2020 Dec 10;63(23):14979-14988. https://pubmed.ncbi.nlm.nih.gov/31902934/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.