# Product data sheet

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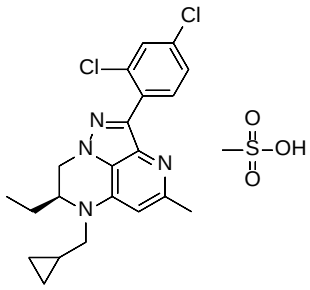
|---|---|
| MedKoo Cat#: 562794<br>Name: NBI-35965 Mesylate<br>CAS: 603151-83-3<br>Chemical Formula: $C_{22}H_{26}Cl_2N_4O_3S$<br>Exact Mass: 496.1103<br>Molecular Weight: 497.435 | |
| Product supplied as: | Powder |
| Purity (by HPLC): | ≥ 98% |
| Shipping conditions | Ambient temperature |
| Storage conditions: | Powder: -20°C 3 years; 4°C 2 years. |
| | In solvent: -80°C 3 months; -20°C 2 weeks. |




**1. Product description:**
NBI-35965 Mesylate is a potent and selective corticotropin-releasing factor receptor 1 (CRF1) antagonist.

**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 |
|---|---|---|
| DMF | 25.0 | 50.26 |
| DMSO | 25.0 | 50.26 |
| Ethanol | 10.0 | 20.10 |

**4. Stock solution preparation table:**

| **Concentration / Solvent Volume / Mass** | **1 mg** | **5 mg** | **10 mg** |
|---|---|---|---|
| 1 mM | 2.01 mL | 10.05 mL | 20.10 mL |
| 5 mM | 0.40 mL | 2.01 mL | 4.02 mL |
| 10 mM | 0.20 mL | 1.01 mL | 2.01 mL |
| 50 mM | 0.04 mL | 0.20 mL | 0.40 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. Gross RS, Guo Z, Dyck B, Coon T, Huang CQ, Lowe RF, Marinkovic D, Moorjani M, Nelson J, Zamani-Kord S, Grigoriadis DE, Hoare SR, Crowe PD, Bu JH, Haddach M, McCarthy J, Saunders J, Sullivan R, Chen T, Williams JP. Design and synthesis of tricyclic corticotropin-releasing factor-1 antagonists. J Med Chem. 2005 Sep 8;48(18):5780-93. doi: 10.1021/jm049085v. PMID: 16134945.
2. Hoare SR, Sullivan SK, Ling N, Crowe PD, Grigoriadis DE. Mechanism of corticotropin-releasing factor type I receptor regulation by nonpeptide antagonists. Mol Pharmacol. 2003 Mar;63(3):751-65. doi: 10.1124/mol.63.3.751. Erratum in: Mol Pharmacol. 2005 Jul;68(1):260. PMID: 12606786.

In vivo study

1. Ma H, Cui Z, Guo X, Zhao Q, Zhang Y, Guan Y, Yang P, Zhu H, Wang S, Zhang X, Zhang Y, Pan HL, Ma H. Corticotropin-releasing factor potentiates glutamatergic input and excitability of presympathetic neurons in the hypothalamus in spontaneously hypertensive rats. Neuropharmacology. 2023 Mar 15;230:109506. doi: 10.1016/j.neuropharm.2023.109506. Epub ahead of print. PMID: 36924924.
2. Kosoyan HP, Grigoriadis DE, Taché Y. The CRF(1) receptor antagonist, NBI-35965, abolished the activation of locus coeruleus neurons induced by colorectal distension and intracisternal CRF in rats. Brain Res. 2005 Sep 14;1056(1):85-96. doi: 10.1016/j.brainres.2005.07.010. PMID: 16095571.

# Product data sheet

**7. Bioactivity**

Biological target:

NBI-35965 Mesylate is a potent and selective corticotropin-releasing factor receptor 1 (CRF1) antagonist.

In vitro activity

As a result of studies aimed at establishing a relationship between structure and CRF(1) binding affinity, NBI 35965 (12a) was identified as a high-affinity antagonist with a pK(i) value of 8.5. Compound 12a proved to be a functional CRF(1) antagonist with pIC(50) values of 7.1 and 6.9 in the in vitro CRF-stimulated cAMP accumulation and ACTH production assays, respectively, and 12a also reduced CRF or stress induced ACTH production in vivo.

Reference: J Med Chem. 2005 Sep 8;48(18):5780-93. https://pubmed.ncbi.nlm.nih.gov/16134945/

In vivo activity

This study examined the influence of repeated phasic CRDs and intracisternal (ic) CRF on the spontaneous discharge rate of LC neurons in chloral hydrate-anesthetized rats and the role of CRF receptors using the nonselective CRF(1)/CRF(2) antagonist, astressin, and the water-soluble CRF(1) receptor antagonist, NBI-35965. NBI-35965 (10 mg/kg, iv) prevented the 2nd CRD- and ic CRF-induced LC neuronal activation, while at 5 mg significantly reduced the LC response to the 2nd CRD by 80%, but did not block that of ic CRF injected 30 min later.

Reference: Brain Res. 2005 Sep 14;1056(1):85-96. https://pubmed.ncbi.nlm.nih.gov/16095571/