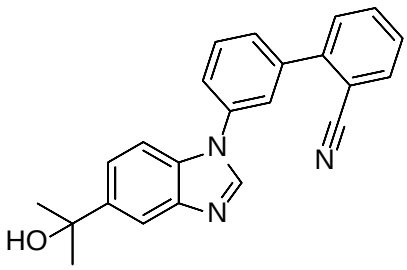
Product data sheet

MedKoo Cat#: 522381 Name: NS-11394 CAS: 951650-22-9 Chemical Formula: $C_{23}H_{19}N_3O$ Exact Mass: 353.1528 Molecular Weight: 353.425	
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:

NS-11394 is a drug which acts as a subtype-selective positive allosteric modulator at GABAA receptors, with selectivity for the α3 and α5 subtypes. NS-11394 has been researched as an analgesic for use in chronic or neuropathic pain. NS-11394 possesses a functional selectivity profile at GABA(A) receptors of alpha(5) > alpha(3) > alpha(2) > alpha(1) based on oocyte electrophysiology with human GABA(A) receptors. Compared with other subtype-selective ligands, NS11394 is unique in having superior efficacy at GABA(A)-alpha(3) receptors while maintaining low efficacy at GABA(A)-alpha(1) receptors. NS11394 has an excellent pharmacokinetic profile, which correlates with pharmacodynamic endpoints (CNS receptor occupancy). NS11394 is potent and highly effective in rodent anxiety models. NS11394 has a significantly reduced side effect profile in rat (sedation, ataxia, and ethanol interaction) and mouse (sedation), even at full CNS receptor occupancy. NS11394 has a unique subtype-selective GABA(A) receptor profile and represents an excellent pharmacological tool to further understanding on the relative contributions of GABA(A) receptor subtypes in various therapeutic areas.

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	33.0	93.37
DMSO	68.0	192.40
Ethanol	52.0	147.13
Ethanol:PBS (pH 7.2) (1:5)	0.16	0.45

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.83 mL	14.15 mL	28.29 mL
5 mM	0.57 mL	2.83 mL	5.66 mL
10 mM	0.28 mL	1.41 mL	2.83 mL
50 mM	0.06 mL	0.28 mL	0.57 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. Mirza NR, Larsen JS, Mathiasen C, Jacobsen TA, Munro G, Erichsen HK, Nielsen AN, Troelsen KB, Nielsen EØ, Ahring PK. NS11394 [3'-[5-(1-hydroxy-1-methyl-ethyl)-benzoimidazol-1-yl]-biphenyl-2-carbonitrile], a unique subtype-selective GABAA receptor positive allosteric modulator: in vitro actions, pharmacokinetic properties and in vivo anxiolytic efficacy. J Pharmacol Exp Ther. 2008 Dec;327(3):954-68. doi: 10.1124/jpet.108.138859. Epub 2008 Sep 12. PMID: 18791063.

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In vivo study

1. Spröte C, Richter F, Bauer A, Gerstenberger J, Richter A. The α2β3γ2 GABAA receptor preferring agonist NS11394 aggravates dystonia in the phenotypic dtsz model. Eur J Pharmacol. 2016 Nov 15;791:655-658. doi: 10.1016/j.ejphar.2016.09.040. Epub 2016 Sep 30. PMID: 27693801.
2. Munro G, Lopez-Garcia JA, Rivera-Arconada I, Erichsen HK, Nielsen EØ, Larsen JS, Ahring PK, Mirza NR. Comparison of the novel subtype-selective GABAA receptor-positive allosteric modulator NS11394 [3'-[5-(1-hydroxy-1-methyl-ethyl)-benzoimidazol-1-yl]-biphenyl-2-carbonitrile] with diazepam, zolpidem, bretazenil, and gaboxadol in rat models of inflammatory and neuropathic pain. J Pharmacol Exp Ther. 2008 Dec;327(3):969-81. doi: 10.1124/jpet.108.144568. Epub 2008 Sep 12. PMID: 18791060.

7. Bioactivity

Biological target:

NS11394 is an orally active and unique subtype-selective GABAA positive allosteric receptor (PAM), with a K_i of ~0.5 nM.

In vitro activity

Specifically, this study show that NS11394 is potent and highly effective in rodent anxiety models. NS11394 impairs memory in both rats and mice, which is possibly attributable to its efficacy at GABA(A)-alpha(5) receptors, albeit activity at this receptor might be relevant to its antinociceptive effects (J Pharmacol Exp Ther 327:doi;10.1124/jpet.108.144, 2008). In conclusion, NS11394 has a unique subtype-selective GABA(A) receptor profile and represents an excellent pharmacological tool to further our understanding on the relative contributions of GABA(A) receptor subtypes in various therapeutic areas.

Reference: J Pharmacol Exp Ther. 2008 Dec;327(3):954-68. https://pubmed.ncbi.nlm.nih.gov/18791063/

In vivo activity

Oral administration of NS11394 (1-30 mg/kg) to rats attenuated spontaneous nociceptive behaviors in response to hindpaw injection of formalin and capsaicin, effects that were blocked by the benzodiazepine site antagonist flumazenil. Ongoing inflammatory nociception, observed as hindpaw weight-bearing deficits after Freund's adjuvant injection, was also completely reversed by NS11394. Likewise, hindpaw mechanical allodynia was fully reversed by NS11394 in two rat models of peripheral neuropathic pain.

Reference: J Pharmacol Exp Ther. 2008 Dec;327(3):969-81. https://pubmed.ncbi.nlm.nih.gov/18791060/

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.