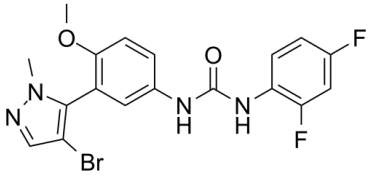
Data Sheet

Product Name:	Nelotanserin
Cat. No.:	CS-5984
CAS No.:	839713-36-9
Molecular Formula:	C18H15BrF2N4O2
Molecular Weight:	437.24
Target:	5-HT Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Solubility:	DMSO : ≥ 32 mg/mL (73.19 mM)



BIOLOGICAL ACTIVITY:

Nelotanserin is a potent **5-HT$_{2A}$** inverse agonist, a moderately potent **5-HT$_{2C}$** partial inverse agonist and a weak **5-HT$_{2B}$** inverse agonist, with **IC$_{50}$s** of 1.7, 79, 791 nM in IP accumulation assays, respectively. **In Vitro:** Results from IP accumulation assays suggest that Nelotanserin is a potent 5-HT$_{2A}$ full inverse agonist (IC$_{50}$=1.7 nM), a moderately potent 5-HT$_{2C}$ partial inverse agonist (IC$_{50}$=79 nM) (maximal response was 62% of the response obtained for the reference inverse agonist clozapine), and a weak 5-HT$_{2B}$ inverse agonist (IC$_{50}$=791 nM). Nelotanserin displays high affinity for recombinant human 5-HT$_{2A}$ receptors (K$_i$=0.35 nM), moderate affinity for human 5-HT$_{2C}$ receptors (K$_i$=100 nM), and low affinity for human 5-HT$_{2B}$ receptors (2000 nM) stably expressed in HEK293 cells. The results suggest that Nelotanserin has a 262-fold higher affinity for human 5-HT$_{2A}$ than 5-HT$_{2C}$ receptors and a 6610-fold higher affinity for human 5-HT$_{2A}$ than 5-HT$_{2B}$ receptors[1]. **In Vivo:** Each compound is tested in a minimum of five rats by oral gavage with administration occurring in the middle of the inactive period, 6 h after light onset. The delta power during non-REM sleep (NREMS) is significantly different between all the analogues tested and the vehicle control. Nelotanserin (Compound 39) produces significant increases in delta power that persist for the first 4 h following dosing. Significant differences are found, however, in NREMS bout length. Nelotanserin significantly increases NREMS bout length during the first hour following dosing, and 3 does so during the second hour. In conjunction with this increased NREM bout duration, the number of NREM bouts decrease during the first hour for Nelotanserin ($p<0.01$) as well as for compound 15 ($p<0.05$)[2].

References:

[1]. Al-Shamma HA et al. Nelotanserin, a novel selective human 5-hydroxytryptamine2A inverse agonist for the treatment of insomnia. J Pharmacol Exp Ther. 2010 Jan;332(1):281-90.

[2]. Teegarden BR et al. Discovery of 1-[3-(4-bromo-2-methyl-2h-pyrazol-3-yl)-4-methoxyphenyl]-3-(2,4-difluorophenyl)urea (nelotanserin) and related 5-hydroxytryptamine2A inverse agonists for the treatment of insomnia. J Med Chem. 2010 Mar 11;53(5):1923-36.

CAIndexNames:

Urea, N-[3-(4-bromo-1-methyl-1H-pyrazol-5-yl)-4-methoxyphenyl]-N'-(2,4-difluorophenyl)-

SMILES:

COC1=C(C2=C(Br)C=NN2C)C=C(NC(NC3=C(F)C=C(F)C=C3)=O)C=C1

Caution: Product has not been fully validated for medical applications. For research use only.

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