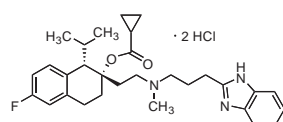


## Available First from Sigma-RBI!

### NNC 55-0396: Selective T-type Ca<sup>2+</sup> channel blocker

Prod. Code **N 0287**



Nonhydrolyzable analog of mibefradil; IC<sub>50</sub> in HEK293 cells is 7 μM. Does not affect the voltage-dependent activation of T-type Ca<sup>2+</sup> currents, but changes the slope of the steady-state inactivation curve.

#### Reference

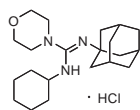
- Huang, L., et al., NNC 55-0396 [(1S,2S)-2-(2-(N-[(3-benzimidazol-2-yl)propyl]-N-methylamino)ethyl)-6-fluoro-1,2,3,4-tetrahydro-1-isopropyl-2-naphthyl cyclopropanecarboxylate dihydrochloride]: a new selective inhibitor of T-type calcium channels. *J. Pharmacol. Exp. Ther.*, **309**, 193-199 (2004).

#### Additional T-type Ca<sup>2+</sup> Channel Blockers

Product Name	Prod. Code
Mibefradil dihydrochloride	M 5441
Penfluridol	P 3371
Kurtoxin	K 1514

### PNU-37883A (U-37883A): Selective vascular ATP-sensitive K<sup>+</sup> K<sub>ir</sub>6.1/SUR2B channel blocker

Prod. Code **P 0248**



Selective blocker (IC<sub>50</sub> = 6 μM) against HEK-293 cells stably expressing putative smooth muscle K<sub>ir</sub>6.1/SUR2B channels [1]; IC<sub>50</sub> = 5 μM against K<sub>ir</sub>6.1/K<sub>ir</sub>6.2 chimeric channels co-expressed with SUR1 in *Xenopus* oocytes [2]. PNU-37883A is more potent than the sulfonylurea drug Glybenclamide (Glyburide)

at inhibiting K<sub>ir</sub>6.1/SUR2B channels expressed in the brain (50-fold, as measured by half-maximal concentration to achieve channel inhibition), kidney (9-fold, as measured by increased urinary sodium excretion), and vascular smooth muscle (6-fold, as measured by a decrease in blood pressure, induced by an ATP-sensitive K<sup>+</sup> channel opener, Pinacidil) [3,4].

#### References

- Cui, Y., et al., Different molecular sites of action for the KATP channel inhibitors, PNU-99963 and PNU-37883A. *Br. J. Pharmacol.*, **139**, 122-128 (2003).
- Kovalev, H., et al., Molecular analysis of the subtype-selective inhibition of cloned KATP channel by PNU-37883A. *Br. J. Pharmacol.*, **141**, 867-873 (2004).
- Ludens, J.H., et al., Renal and vascular effects on chemically distinct ATP-sensitive K<sup>+</sup> channel blockers in rats. *J. Cardiovasc. Pharmacol.*, **25**, 404-409 (1995).
- Lin, Y.-J., et al., U-37883A potently inhibits dopamine-modulated K<sup>+</sup> channels on rat striatal neurons. *Eur. J. Pharmacol.*, **352**, 335-341 (1998).

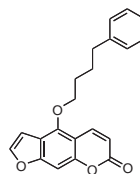
#### Related Products

Product Name	Descriptor	Prod. Code
Glybenclamide	Selective ATP-sensitive K <sup>+</sup> channel blocker	G 0639
Pinacidil	K <sup>+</sup> channel activator	P-154

## Available First from Sigma-RBI!

### Psora-4: Potent K<sub>v</sub>1.3 K<sup>+</sup> channel blocker

Prod. Code **P 9872**



Psora-4 is the most potent blocker of K<sub>v</sub>1.3 K<sup>+</sup> channels described to date. It blocks these channels in a use-dependent manner displaying an EC<sub>50</sub> value of 3 nM, and exhibits 17- to 70-fold selectivity for K<sub>v</sub>1.3 over K<sub>v</sub>1.1, K<sub>v</sub>1.2, K<sub>v</sub>1.4 and K<sub>v</sub>1.7. It shows no effect on the ether-a-go-go-related channel, K<sub>v</sub>3.1, the Ca<sup>2+</sup>-activated K<sup>+</sup> channels or neuronal Nav1.2 channels. It

has been shown to suppress proliferation of human and rat myelin-specific effector memory T-cells displaying EC<sub>50</sub> values of 25 nM and 60 nM, respectively.

#### References

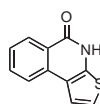
- Vennekamp, J., et al., Kv1.3-blocking 5-phenylalkoxy-psoralens: a new class of immunomodulators. *Mol. Pharmacol.*, **65**, 1364-1374 (2004).
- Chandy, K.G., et al., K<sup>+</sup> channels as targets for specific immunomodulation. *Trends Pharmacol. Sci.*, **25**, 280-289 (2004).

#### Additional K<sup>+</sup> Channel Blockers

Product Name	Prod. Code
Agitoxin-1, recombinant, expressed in <i>E. coli</i>	A 5229
Margatoxin from <i>Centruoides margaritatus</i> (scorpion)	M 8278
Margatoxin from <i>Centruoides margaritatus</i> (scorpion) recombinant, expressed in <i>E. coli</i>	M 8437

### TIQ-A: Poly(ADP-Ribose) polymerase (PARP) inhibitor

Prod. Code **T 2825**



Cell permeable, potent PARP inhibitor; IC<sub>50</sub> of 450 nM versus recombinant bovine PARP-1; shown to be neuroprotective against oxygen-glucose deprivation injury *in vitro* in cultured murine cortical cells (IC<sub>50</sub> = 150 nM) and *in vivo* in rat transient focal ischemia model (3 mg/kg ip).

#### References

- Chiarugi A, et al., Novel isoquinolinone-derived inhibitors of poly(ADP-ribose) polymerase-1: pharmacological characterization and neuroprotective effects in an *in vitro* model of cerebral ischemia. *J. Pharmacol. Exp. Ther.*, **305**, 943-949 (2003).
- Pellicciari, R., et al., Towards new neuroprotective agents: design and synthesis of 4H-thieno[2,3-c] isoquinolin-5-one derivatives as potent PARP-1 inhibitors. *Farmacol.*, **58**, 851-858 (2003).

#### Additional PARP Inhibitors

Product Name	Prod. Code
3-Aminobenzamide	A 0788
4-Amino-1,8-naphthalimide	A 0966
DPQ	D 5314
1,5-Isoquinolinediol	I-138
PJ-34	P 4365
6(SH)-Phenanthridinone	P 8852