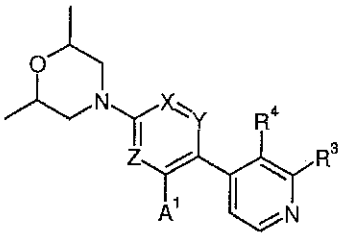
CLAIMS

1. A compound of the formula (Ia), or a pharmaceutically acceptable salt thereof:



(Ia)

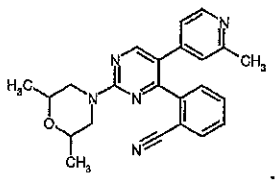
wherein:

- X, Y and Z are each independently selected from CH and N;
- A^1 is selected from a isobutyl and a 5 or 6-membered aryl or heteroaryl, wherein said 5 or 6-membered aryl or heteroaryl is selected from a carbon-linked phenyl, pyridinyl, pyrimidinyl, furyl, pyrrolyl, thienyl or isoxazolyl, each optionally substituted with one or two substituents independently selected from halo, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy; and
- one of R^3 and R^4 is hydrogen and the other is methyl.

2. A compound according to claim 1 wherein Y is CH.

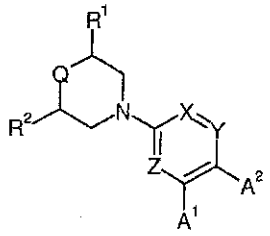
3. The compound according to claim 1 or claim 2, or a pharmaceutically acceptable salt thereof, wherein A^1 is selected from isobutyl, phenyl, carbon-linked pyridinyl or carbon-linked furyl, said phenyl, pyridinyl or furyl each optionally substituted with one or two substituents independently selected from halo, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy.

4. The compound according to any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein the compound is other than:



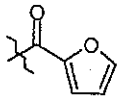
5. A compound of formula (Ia) which is:
cis-4-[4-(6-Fluoro-4-methyl-3-pyridinyl)-5-(2-methyl-4-pyridinyl)-2-pyrimidinyl]-2,6-dimethylmorpholine, or a pharmaceutically acceptable salt thereof.

6. A compound of formula (I) or a salt thereof:



(I)

for use in treating diseases and conditions mediated by modulation of the α7 nicotinic acetyl choline receptor (nAChR), wherein:

- X, Y and Z are each independently selected from CH and N;
- A^1 is isobutyl or a 5 or 6-membered aryl or heteroaryl selected from a carbon-linked phenyl, pyridinyl, pyrimidinyl, furyl, pyrrolyl, thienyl or isoxazolyl, each optionally substituted with one or two substituents independently selected from halo, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy, and A^2 is a 5 or 6-membered heteroaryl selected from a carbon-linked pyridinyl, pyrimidinyl, furyl, pyrrolyl, thienyl or isoxazolyl, each optionally substituted with one or two substituents independently selected from halo, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy;
- Q is selected from a bond, $-CH_2-$, $-CH_2CH_2-$, -O-, -S- and $-N(R^a)-$, wherein R^a is ;
- R^1 and R^2 are each individually selected from hydrogen and methyl, with the proviso that when Q is –O-, then R^1 and R^2 are both methyl.

or a pharmaceutically acceptable salt thereof.

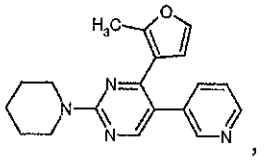
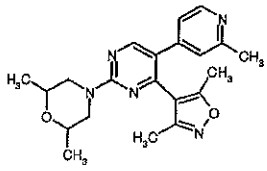
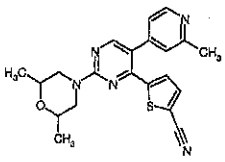
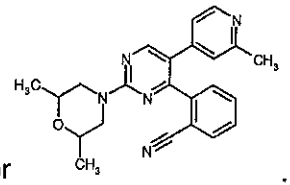
7. A compound according to claim 6 wherein Y is CH.

8. A compound according to claim 6 or 7 wherein the diseases and conditions mediated by modulation of the α7 nicotinic acetyl choline receptor (nAChR) are pain, a psychotic disorder, cognitive impairment or Alzheimer's disease

9. The compound according to any one of claims 6 to 8, or a pharmaceutically acceptable salt thereof, wherein A^2 is pyridinyl optionally substituted with one methyl group.

10. The compound according to any one of claims 6 to 9, or a pharmaceutically acceptable salt thereof, wherein either: Q is selected from a bond, $-CH_2CH_2-$ and -S-, and R^1 and R^2 are both H; Q is $-CH_2-$, R^1 is selected from H and methyl and R^2 is H; or Q is -O- and R^1 and R^2 are both methyl.

11. The compound according to any one of claims 6 to 10 or a pharmaceutically acceptable salt thereof, wherein the compound is other than:

, ,  or .

12. A compound which is:

4-(2-Methyl-3-furanyl)-2-(3-methyl-1-piperidinyl)-5-(4-pyridinyl)pyrimidine ;

4-(2-Methyl-3-furanyl)-2-(3-methyl-1-piperidinyl)-5-(3-pyridinyl)pyrimidine;

4-(2-Methyl-3-furanyl)-2-(3-methyl-1-piperidinyl)-5-(2-methyl-4-pyridinyl)pyrimidine;

4-(2-Methyl-3-furanyl)-5-(2-methyl-4-pyridinyl)-2-(1-piperidinyl)pyrimidine;

cis-2,6-Dimethyl-4-[4-(2-methyl-3-furanyl)-5-(2-methyl-4-pyridinyl)-2-pyrimidinyl]morpholine;

trans-2,6-Dimethyl-4-[4-(2-methyl-3-furanyl)-5-(2-methyl-4-pyridinyl)-2-pyrimidinyl]morpholine;

1-[4-(2-Methyl-3-furanyl)-5-(2-pyridinyl)-2-pyrimidinyl]hexahydro-1*H*-azepine;

4-(2-Methyl-3-furanyl)-2-(3-methyl-1-piperidinyl)-5-(2-pyridinyl)pyrimidine;

cis-2,6-Dimethyl-4-[4-(2-methylpropyl)-5-(2-methyl-4-pyridinyl)-2-pyrimidinyl]morpholine;

cis-2,6-Dimethyl-4-[6-(2-methyl-3-furanyl)-5-(2-methyl-4-pyridinyl)-2-pyrazinyl]morpholine;

6-(*cis*-2,6-dimethyl-4-morpholinyl)-2'-methyl-4-(2-methyl-3-furanyl)-3,4'-bipyridine;

6-(*cis*-2,6-dimethyl-4-morpholinyl)-2'-methyl-2-(2-methyl-3-furanyl)-3,4'-bipyridine;

cis-2,6-Dimethyl-4-[3-(2-methyl-3-furanyl)-4-(2-methyl-4-pyridinyl)phenyl]morpholine;

cis-2,6-Dimethyl-4-[4-(2-methylphenyl)-5-(2-methyl-4-pyridinyl)-2-pyrimidinyl]morpholine;

cis-2,6-dimethyl-4-[4-(2-methyl-3-furanyl)-5-(3-methyl-4-pyridinyl)-2-pyrimidinyl]morpholine;

cis-2,6-Dimethyl-4-{5-(2-methyl-4-pyridinyl)-4-[2-(trifluoromethyl)-3-pyridinyl]-2-pyrimidinyl}morpholine;

cis-4-[4-(6-Fluoro-4-methyl-3-pyridinyl)-5-(2-methyl-4-pyridinyl)-2-pyrimidinyl]-2,6-dimethylmorpholine;
cis-2-[2-(2,6-Dimethyl-4-morpholinyl)-5-(2-methyl-4-pyridinyl)-4-pyrimidinyl]-4-fluorobenzonitrile;
cis-2-[2-(2,6-dimethyl-4-morpholinyl)-5-(2-methyl-4-pyridinyl)-4-pyrimidinyl]-6-(trifluoromethyl)benzonitrile,
or a pharmaceutically acceptable salt thereof.

13. A compound as defined in any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, for use as a medicament.

14. A compound as defined in any one of claims 1 to 12 or a pharmaceutically acceptable salt thereof, for use in the treatment of pain, a psychotic disorder, cognitive impairment or Alzheimer's disease.

15. Use of a compound as defined in any one of claims 1 to 12 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of pain, a psychotic disorder, cognitive impairment or Alzheimer's disease.

16. The compound or a pharmaceutically acceptable salt thereof according to claim 14 or the use according to claim 14, wherein the psychotic disorder is schizophrenia.

17. The compound or a pharmaceutically acceptable salt thereof according to claim 14 or the use according to claim 15, wherein the pain is neuropathic pain.

~~18. A method of treating pain, a psychotic disorder, cognitive impairment or Alzheimer's disease in a human comprising administering an effective amount of a compound of claim 1 or claim 6, or a pharmaceutically acceptable salt thereof.~~

~~19. A method of treating schizophrenia in a human comprising administering an effective amount of a compound of claim 1 or claim 6, or a pharmaceutically acceptable salt thereof.~~

~~20. A method of treating neuropathic pain in a human comprising administering an effective amount of a compound of claim 1 or claim 6, or a pharmaceutically acceptable salt thereof.~~

~~21.~~18. A pharmaceutical composition comprising:

a) a compound as defined in any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof; and

b.) one or more pharmaceutically acceptable carriers or excipients.

~~22.~~ 19. The pharmaceutical composition of claim 21, further comprising:

c.) an additional therapeutic agent.