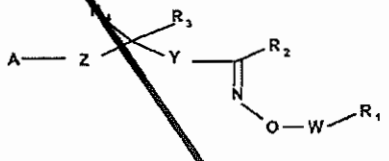
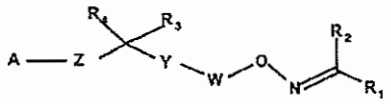
Claims

1. A compound of formula A1 or A2 for use in the treatment of a demyelinating peripheral neuropathy:



A1



A2

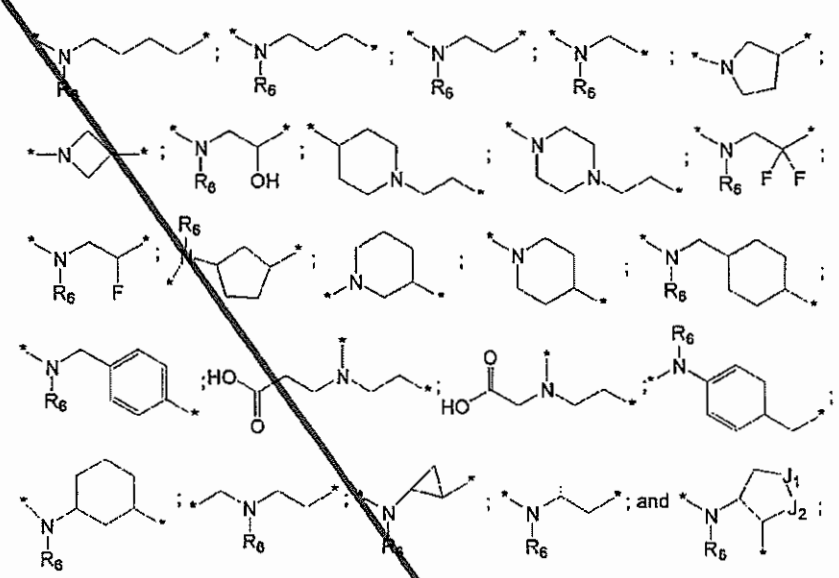
wherein

A is $COOR_5$, $OPO(OR_5)_2$, $PO(OR_5)_2$, SO_2OR_5, POR_5OR_5 or 1*H*-tetrazol-5-yl, R_5 being H or an ester-forming group, optionally C_{1-6}alkyl;

W is a bond, C_{1-3}alkylene or C_{2-3}alkenylene;

Y is C_{6-10}aryl or C_{2-9}heteroaryl eg C_{3-9}heteroaryl, optionally substituted by 1 to 3 radicals selected from halogen, OH, NO_2, C_{1-6}alkyl, C_{1-6}alkoxy; halo-substituted C_{1-6}alkyl and halo-substituted
C_{1-6}alkoxy;

Z is chosen from:



wherein the left and right asterisks of Z indicate the point of attachment between -C(R_3)(R_4)- and A of Formula Ia or Ib, respectively; R_6 is chosen from hydrogen and C_{1-6}alkyl; and J_1 and J_2 are independently methylene or a heteroatom chosen from S, O and NR_5; wherein R_5 is chosen from hydrogen and C_{1-6}alkyl; and any alkylene of Z can be further substituted by one to three radicals chosen from halo, hydroxy, C_{1-6}alkyl; or R_6 can be attached to a carbon atom of Y to form a 5-7 member ring;

R_1 is C_{6-10}aryl or C_{2-9}heteroaryl eg C_{3-9}heteroaryl, optionally substituted by C_{1-6}alkyl, C_{6-10}aryl, C_{6-10}arylC_{1-4}alkyl, C_{3-9}heteroaryl, C_{3-9}heteroarylC_{1-4}alkyl, C_{3-8}cycloalkyl, C_{3-8}cycloalkylC_{1-4}alkyl, C_{3-8}heterocycloalkyl or C_{3-8}heterocycloalkylC_{1-4}alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl of R_1 may be substituted by 1 to 5 groups selected from halogen, C_{1-6}alkyl, C_{1-6}alkoxy and halo substituted-C_{1-6}alkyl or -C_{1-6}alkoxy;

R_2 is H, C_{1-6}alkyl, halo substituted C_{1-6}alkyl, C_{2-6}alkenyl or C_{2-6}alkynyl; and

each of R_3 and R_4, independently, is H, halogen, OH, C_{1-6}alkyl, C_{1-6}alkoxy or halo substituted C_{1-6}alkyl or C_{1-6}alkoxy;

and the N-oxide derivatives thereof or prodrugs thereof,
or a pharmacologically acceptable salt, solvate or hydrate thereof.

2. A compound of claim 1, wherein the neuropathy is Guillain-Barré syndrome.

3. A compound of claim 1, wherein the neuropathy is chronic inflammatory demyelinating polyradiculoneuropathy.

4. A compound of claim 1, wherein the neuropathy is multifocal motor neuropathy with conduction block.

5. A compound of claim 1, wherein the neuropathy is paraproteinaemic demyelinating peripheral neuropathy.

6. A compound of any preceding claim, wherein A is $COOR_5$.

7. A compound of claim 6, wherein A is COOH.

8. A compound of any preceding claim, wherein W is ethylene.

9. A compound of any preceding claim, wherein Y is optionally substituted phenyl or C_6heteroaryl.

10. A compound of any of claims 1 to 8, wherein Y is C_{6-10}aryl or C_{3-9}heteroaryl, substituted with a single C_{1-6}alkyl substituent.

11. A compound of claim 10, wherein Y is phenyl optionally substituted by ethyl.

12. A compound of any preceding claim, wherein Z is selected from the heterocycles azetidine, pyrrolidine or piperidine, joined to the remainder of the molecule at the 1- and 3-positions; or piperidine joined to the remainder of the molecule at the 1- and 4- positions; optionally wherein the heterocycle is N-substituted (1-substituted) by moiety A and substituted at the 3 or, as the case may be, 4-position by $-C(R_3)(R_4)-$.

13. A compound of any preceding claim, wherein R_1 is optionally substituted phenyl or optionally substituted C_6heteroaryl.

14. A compound of any preceding claim, wherein R_1 has two substituents selected from optionally halo-substituted alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, optionally halo-substituted phenyl and optionally halo-substituted C_{3-8}cycloalkyl.

15. A compound of claim 14 wherein R_1 is phenyl or C_6heteroaryl.

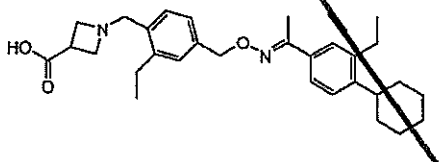
16. A compound of claim 15, wherein R_1 has one optionally halo-substituted alkyl group and one optionally halo-substituted cyclic moiety selected from phenyl and C_{3-8}cycloalkyl groups.

17. A compound of any preceding claim, wherein R_2 is methyl.

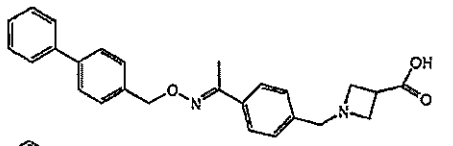
18. A compound of any preceding claim, wherein R_3 and R_4 are each independently H, halogen, methyl or halo-substituted methyl.

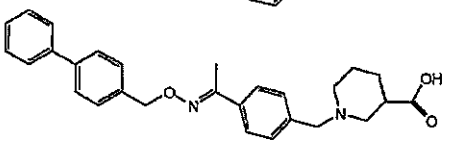
19. A compound of claim 18, wherein R_3 and R_4 are both H.

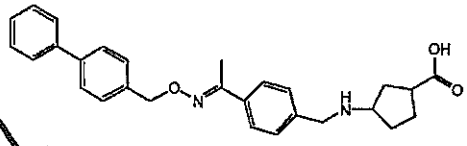
20. A compound of any of claims 1 to 5, wherein the compound is selected from:

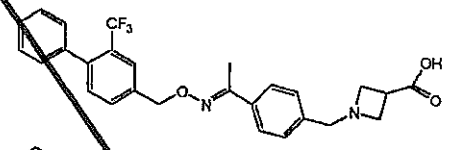


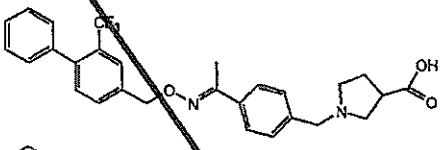
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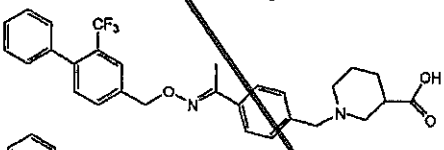

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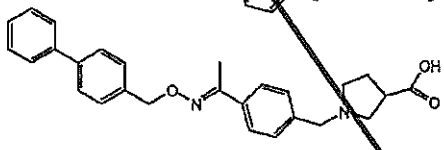

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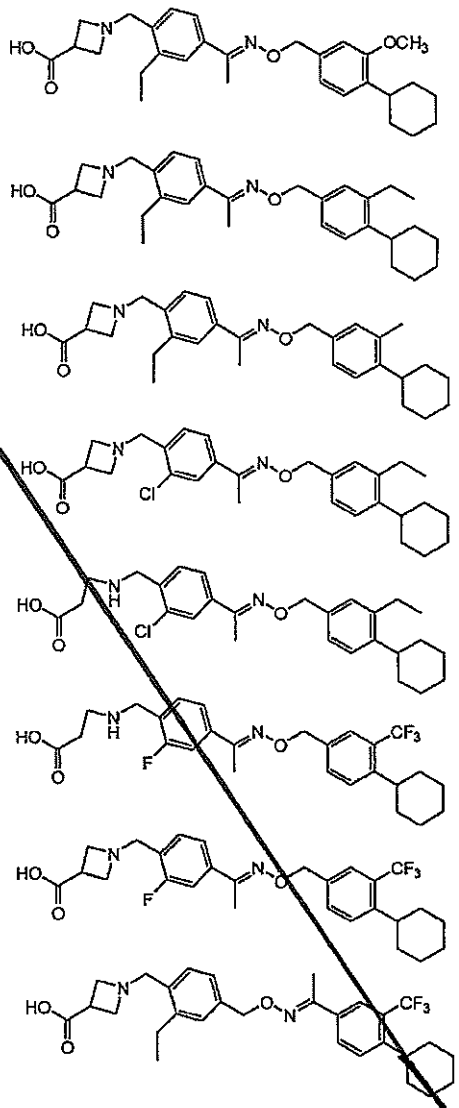

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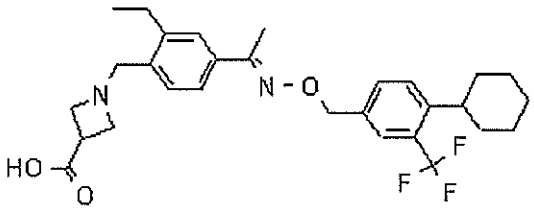

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21. A compound of any of claims 1 to 5, wherein the compound is 1-{4-[1-(4-Cyclohexyl-3-trifluoromethyl-benzyloxyimino)-ethyl]-2-ethyl-benzyl}-azetidine-3-carboxylic acid:



22. A method of treating a subject having a demyelinating peripheral neuropathy comprising administering to the subject an effective amount of a compound having a structure defined in any of claims 1 and 6 to 21.

23. A method of alleviating a symptom of, delaying the progression of, or prolonging time to relapse of a demyelinating peripheral neuropathy comprising administering to the subject an effective amount of a compound having a structure defined in any of claims 1 and 6 to 21.

24. A method of improving or maintaining, or delaying the deterioration of, the status of a subject having a demyelinating peripheral neuropathy comprising administering to the subject an effective amount of a compound having a structure defined in any of claims 1 and 6 to 21.

25. A method of claim 22, 23 or 24, wherein the neuropathy is Guillain-Barré syndrome.

26. A method of claim 22, 23 or 24, wherein the neuropathy is chronic inflammatory demyelinating polyradiculoneuropathy.

27. A method of claim 22, 23 or 24, wherein the neuropathy is multifocal motor neuropathy with conduction block.

28. A method of claim 22, 23 or 24, wherein the neuropathy is paraproteinaemic demyelinating peripheral neuropathy.

29. A pharmaceutical formulation comprising a compound having a structure defined in any of claims 1 and 6 to 21 in combination with at least one further therapeutic agent useful for treating a patient having a demyelinating peripheral neuropathy.

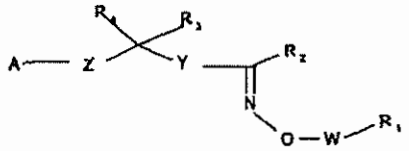
30. A formulation of claim 29, wherein the at least one further therapeutic agent is selected from an immunosuppresant (e.g., cyclosporin A, cyclosporin G, FK-506, ABT-281, ASM981, rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, a corticosteroid, cyclophosphamide, azathioprine, methotrexate, leflunomide, mizoribine, mycophenolate mofetil, or 15-

deoxyspergualine), a steroid (e.g., prednisone or hydrocortisone), an immunoglobulin, or type 1 interferon.

31. A compound having a structure defined in any of claims 1 and 6 to 21 for simultaneous, separate or sequential co-administration with at least one further agent as defined in claim 29 or 30.

Claims

1. Use of compound of formula A1:



A1

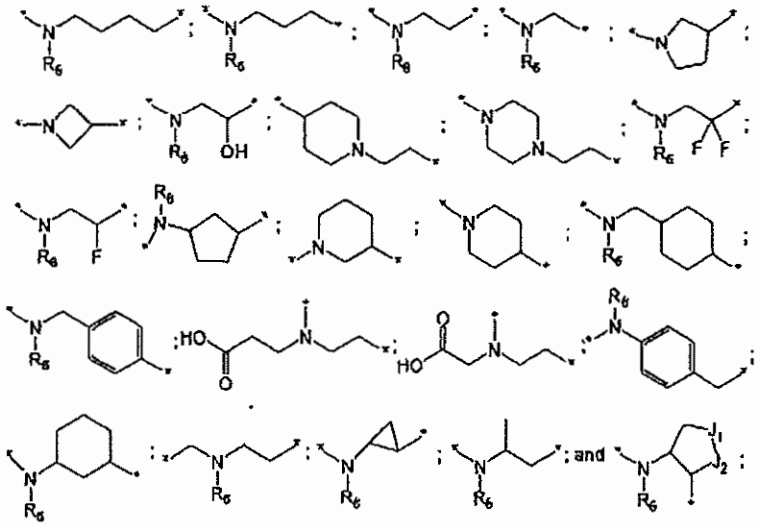
wherein

A is $COOR_5$, $OPO(OR_5)_2$, $PO(OR_5)_2$, SO_2OR_5, POR_5OR_5 or 1*H*-tetrazol-5-yl, R_5 being H or an ester-forming group;

W is a bond, C_{1-3}alkylene or C_{2-3}alkenylene;

Y is C_{6-10}aryl or C_{2-9}heteroaryl, optionally substituted by 1 to 3 radicals selected from halogen, OH, NO_2, C_{1-6}alkyl, C_{1-6}alkoxy; halo-substituted C_{1-6}alkyl and halo-substituted C_{1-6}alkoxy;

Z is chosen from:



wherein the left and right asterisks of Z indicate the point of attachment between -$C(R_3)(R_4)$- and A of Formula Ia or Ib, respectively; R_6 is chosen from hydrogen and C_{1-6}alkyl; and J_1 and J_2 are independently methylene or a heteroatom chosen from S, O and NR_5; wherein R_5 is chosen from hydrogen and C_{1-6}alkyl; and any alkylene of Z can be

further substituted by one to three radicals chosen from halo, hydroxy, C_{1-6}alkyl; or R_6 can be attached to a carbon atom of Y to form a 5-7 member ring;

R_1 is C_{6-10}aryl or C_{2-9}heteroaryl, optionally substituted by C_{1-6}alkyl, C_{6-10}aryl, C_{6-10}arylC_{1-4}alkyl, C_{3-9}heteroaryl, C_{3-9}heteroarylC_{1-4}alkyl, C_{3-8}cycloalkyl, C_{3-8}cycloalkylC_{1-4}alkyl, C_{3-8}heterocycloalkyl or C_{3-8}heterocycloalkylC_{1-4}alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl of R_1 may be substituted by 1 to 5 groups selected from halogen, C_{1-6}alkyl, C_{1-6}alkoxy and halo substituted-C_{1-6}alkyl or -C_{1-6}alkoxy;

R_2 is H, C_{1-6}alkyl, halo substituted C_{1-6}alkyl, C_{2-6}alkenyl or C_{2-6}alkynyl; and

each of R_3 and R_4, independently, is H, halogen, OH, C_{1-6}alkyl, C_{1-6}alkoxy or halo substituted C_{1-6}alkyl or C_{1-6}alkoxy;

or the N-oxide derivative thereof or prodrug thereof, or a pharmacologically acceptable salt, solvate or hydrate thereof; in the manufacture of a medicament for the treatment of a demyelinating peripheral neuropathy selected from chronic inflammatory demyelinating polyradiculoneuropathy, multifocal motor neuropathy with conduction block or paraproteinaemic demyelinating peripheral neuropathy.

2. Use of claim 1, wherein in the compound of formula A1, A is $COOR_5$.

3. Use of claim 1 or claim 2, wherein in the compound of formula A1, Y is optionally substituted phenyl or C_6heteroaryl.

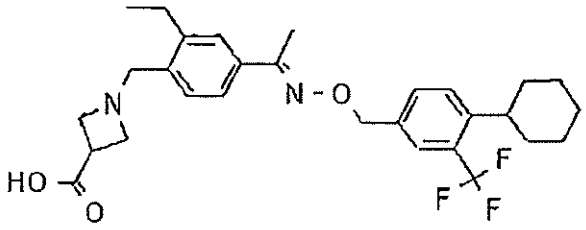
4. Use of any one of claims 1 to 3, wherein in the compound of formula A1, Z is selected from the heterocycles azetidine, pyrrolidine or piperidine, joined to the remainder of the molecule at the 1- and 3- positions; or piperidine joined to the remainder of the molecule at the 1- and 4- positions; optionally wherein the heterocycle is N-substituted (1-substituted) by moiety A and substituted at the 3 or, as the case may be, 4-position by –$C(R_3)(R_4)$-.

5. Use of any one of claims 1 to 4, wherein in the compound of formula A1, R_1 is optionally substituted phenyl or optionally substituted C_6heteroaryl.

6. Use of any one of claims 1 to 5, wherein in the compound of formula A1, R_2 is methyl.

7. Use of any one of claims 1 to 6, wherein in the compound of formula A1, R_3 and R_4 are both H.

8. Use according to claim 1, wherein the compound is 1-{4-[1-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-ethyl]-2-ethyl-benzyl}-azetidine-3-carboxylic acid:



or a pharmacologically acceptable salt thereof.

9. Use of a compound having a structure defined in any one of claims 1 to 8, or a N-oxide derivative thereof or prodrug thereof, or a pharmaceutically acceptable salt, solvate or hydrate thereof in the manufacture of a medicament for alleviating a symptom of, delaying the progression of, or prolonging time to relapse of a demyelinating peripheral neuropathy selected from chronic inflammatory demyelinating polyradiculoneuropathy, multifocal motor neuropathy with conduction block or paraproteinaemic demyelinating peripheral neuropathy.

10. Use of a compound having a structure defined in any one of claims 1 to 8, or a N-oxide derivative thereof or prodrug thereof, or a pharmaceutically acceptable salt, solvate or hydrate thereof in the manufacture of a medicament for improving or maintaining, or delaying the deterioration of, the status of a subject having a demyelinating peripheral neuropathy selected from chronic inflammatory demyelinating polyradiculoneuropathy, multifocal motor neuropathy with conduction block or paraproteinaemic demyelinating peripheral neuropathy.