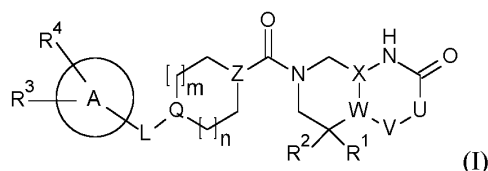


CLAIMS

1. A compound of formula (I)



or a pharmaceutically acceptable salt thereof,

5 wherein:

- (i) U is CH₂;

V is O;

W and X are both CH;

R¹ is selected from halogen and C₁₋₆-alkyl; and

10 R² is selected from hydrogen, halogen, and C₁₋₆-alkyl; or

R¹ and R², taken together with the carbon atom to which they are attached,
form a C₃-C₁₀-cycloalkyl; or

- (ii) U is CH₂;

V is O;

15 W is CR^w;

X is CH;

R^w is selected from halogen, and C₁₋₆-alkyl;

R¹ and R² are independently selected from hydrogen, halogen, and C₁₋₆-alkyl;

or

20 R¹ and R², taken together with the carbon atom to which they are attached,
form a C₃-C₁₀-cycloalkyl; or

- (iii) U is CH₂;

V is O;

W and X together form a group C=C; and

25 R¹ and R² are independently selected from hydrogen, halogen, and C₁₋₆-alkyl;

or

R¹ and R², taken together with the carbon atom to which they are attached,
form a C₃-C₁₀-cycloalkyl; or

- (iv) U is CH₂;

30 V is selected from NH, CH₂, S, S=O, SO₂, CHOH, CHF, and CF₂;

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- (a) W is CR^w; and
X is CH; or
- (b) W and X together form a group C=C;
R^w is selected from hydrogen, halogen, and C₁₋₆-alkyl;
- 5 R¹ and R² are independently selected from hydrogen, halogen, and C₁₋₆-alkyl;
or
R¹ and R², taken together with the carbon atom to which they are attached,
form a C₃-C₁₀-cycloalkyl; or
- (v) U and V together form a group C=C;
- 10 W and X together form a group C=C; and
R¹ and R² are independently selected from hydrogen, halogen, and C₁₋₆-alkyl;
or
R¹ and R², taken together with the carbon atom to which they are attached,
form a C₃-C₁₀-cycloalkyl; or
- 15 (vi) U is CH₂;
V is O;
W is CH;
X is C-OH; and
R¹ and R² are independently selected from hydrogen, halogen, and C₁₋₆-alkyl;
- 20 or
R¹ and R², taken together with the carbon atom to which they are attached,
form a C₃-C₁₀-cycloalkyl;
- m and n are both 0; or
m and n are both 1;
- 25 Z is CH or N;
Q is CR^q or N;
R^q is selected from hydrogen, halogen, hydroxy, halo-C₁₋₆-alkyl, and C₁₋₆-alkyl.
L is selected from a covalent bond, -CHR⁵-, -O-, -OCH₂-, -CH₂O-, -CH₂OCH₂-,
-CF₂CH₂-, and -CH₂CF₂-;
- 30 A is selected from C₆-C₁₄-aryl, 5- to 14-membered heteroaryl, and 3- to 14-
membered heterocyclyl;
R³ and R⁴ are independently selected from hydrogen, halogen, SF₅, cyano, C₁₋₆-
alkyl, C₁₋₆-alkoxy, halo-C₁₋₆-alkyl, halo-C₁₋₆-alkoxy, C₆-C₁₄-aryl, C₃-C₁₀-
cycloalkyl, 5-14-membered heteroaryl, C₆-C₁₄-aryloxy, C₃-C₁₀-cycloalkyloxy,

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- and 5-14-membered heteroaryloxy, wherein said C₆-C₁₄-aryl, C₃-C₁₀-cycloalkyl, 5-14-membered heteroaryl, C₆-C₁₄-aryloxy, C₃-C₁₀-cycloalkyloxy, and 5-14-membered heteroaryloxy, are optionally substituted with 1-2 substituents selected from halogen, C₁₋₆-alkyl, and halo-C₁₋₆-alkyl; and
- 5 R⁵ is selected from hydrogen and C₆-C₁₄-aryl.
2. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:
- (i) U is CH₂;
V is O;
10 W and X are both CH;
R¹ is selected from halogen and C₁₋₆-alkyl; and
R² is selected from hydrogen and halogen; or
- (ii) U is CH₂;
V is O;
15 W and X together form a group C=C; and
R¹ and R² are both hydrogen; or
- (iii) U is CH₂;
V is selected from NH, S, and CH₂;
(a) W and X are both CH; or
20 (b) W and X together form a group C=C; and
R¹ and R² are both hydrogen;
- (iv) U and V together form a group C=C;
W and X together form a group C=C; and
R¹ and R² are both hydrogen; or
- 25 (v) U is CH₂;
V is O;
W is CH;
X is C-OH; and
R¹ and R² are both hydrogen.
- 30 3. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein
- (i) U is CH₂;
V is O;

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- W and X are both CH;
R¹ is selected from halogen and C₁₋₆-alkyl; and
R² is selected from hydrogen and halogen; or
- (ii) U is CH₂;
5 V is NH;
W and X are both CH; and
R¹ and R² are both hydrogen; or
- (iii) U and V together form a group C=C;
W and X together form a group C=C; and
10 R¹ and R² are both hydrogen.
4. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein
- (i) U is CH₂;
V is O;
15 W and X are both CH;
R¹ is selected from fluoro and methyl; and
R² is selected from hydrogen and fluoro; or
- (ii) U is CH₂;
V is NH;
20 W and X are both CH; and
R¹ and R² are both hydrogen; or
- (iii) U and V together form a group C=C;
W and X together form a group C=C; and
R¹ and R² are both hydrogen.
- 25 5. The compound of formula I according to any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein Z is N.
6. The compound of formula I according to any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein Q is CH.
7. The compound of formula I according to any one of claims 1-6, or a
30 pharmaceutically acceptable salt thereof, wherein m and n are both 0.

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8. The compound of formula I according to any one of claims 1-7, or a pharmaceutically acceptable salt thereof, wherein L is selected from a covalent bond, $-\text{CHR}^5-$, and $-\text{CH}_2\text{O}-$.
9. The compound of formula I according to any one of claims 1-7, or a pharmaceutically acceptable salt thereof, wherein L is selected from a covalent bond and $-\text{CH}_2\text{O}-$.
10. The compound of formula I according to any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein A is $\text{C}_6\text{-C}_{14}$ -aryl.
11. The compound of formula I according to any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein A is phenyl.
12. The compound of formula I according to any one of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from hydrogen and halo- $\text{C}_1\text{-C}_6$ -alkyl.
13. The compound of formula I according to any one of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein R^3 is halo- $\text{C}_1\text{-C}_6$ -alkyl.
14. The compound of formula I according to any one of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from CF_3 and 2,2,2-trifluoroethyl.
15. The compound of formula I according to any one of claims 1-14, or a pharmaceutically acceptable salt thereof, wherein R^4 is selected from hydrogen and halogen.
16. The compound of formula I according to any one of claims 1-14, or a pharmaceutically acceptable salt thereof, wherein R^4 is selected from hydrogen and fluoro.
17. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:
 - (i) U is CH_2 ;
 - V is O;
 - W and X are both CH;

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- R^1 is selected from halogen and C_{1-6} -alkyl; and
 R^2 is selected from hydrogen and halogen; or
- (ii) U is CH_2 ;
V is O;
- 5 W and X together form a group $C=C$; and
 R^1 and R^2 are both hydrogen; or
- (iii) U is CH_2 ;
V is selected from NH, S, and CH_2 ;
- (a) W and X are both CH; or
- 10 (b) W and X together form a group $C=C$; and
 R^1 and R^2 are both hydrogen;
- (iv) U and V together form a group $C=C$;
W and X together form a group $C=C$; and
 R^1 and R^2 are both hydrogen; or
- 15 (v) U is CH_2 ;
V is O;
W is CH;
X is C-OH; and
 R^1 and R^2 are both hydrogen;
- 20 Z is N;
Q is CH;
m and n are both 0;
L is selected from a covalent bond, $-CHR^5-$, and $-CH_2O-$;
A is C_6-C_{14} -aryl;
- 25 R^3 is selected from hydrogen and halo- C_1-C_6 -alkyl;
 R^4 is selected from hydrogen and halogen; and
 R^5 is selected from hydrogen and C_6-C_{14} -aryl.
18. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein
- 30 (i) U is CH_2 ;
V is O;
W and X are both CH;
 R^1 is selected from halogen and C_{1-6} -alkyl; and

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- R² is selected from hydrogen and halogen; or
- (ii) U is CH₂;
V is NH;
W and X are both CH; and
5 R¹ and R² are both hydrogen; or
- (iii) U and V together form a group C=C;
W and X together form a group C=C; and
R¹ and R² are both hydrogen;
Z is N;
10 Q is CH;
m and n are both 0;
L is selected from a covalent bond and -CH₂O-;
A is C₆-C₁₄-aryl;
R³ is halo-C₁-C₆-alkyl; and
15 R⁴ is selected from hydrogen and halogen.
19. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein
- (i) U is CH₂;
V is O;
20 W and X are both CH;
R¹ is selected from fluoro and methyl; and
R² is selected from hydrogen and fluoro; or
- (ii) U is CH₂;
V is NH;
25 W and X are both CH; and
R¹ and R² are both hydrogen; or
- (iii) U and V together form a group C=C;
W and X together form a group C=C; and
R¹ and R² are both hydrogen;
30 Z is N;
Q is CH;
m and n are both 0;
L is selected from a covalent bond and -CH₂O-;

A is phenyl;

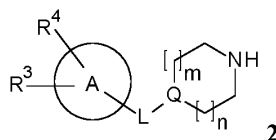
R³ is selected from CF₃ and 2,2,2-trifluoroethyl; and

R⁴ is selected from hydrogen and fluoro.

20. A compound of formula (I) according to any one of claims 1 to 19, or a
5 pharmaceutically acceptable salt thereof, selected from:
rel-(4aR,8S,8aS)-6-[3-[[2-Fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-
carbonyl]-8-methyl-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
rel-(4aS,8R,8aR)-6-[3-[[2-Fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-
carbonyl]-8-methyl-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
10 rel-(4aS,8aS)-8,8-Difluoro-6-[3-[[2-fluoro-4-
(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-4a,5,7,8a-tetrahydro-4H-
pyrido[4,3-b][1,4]oxazin-3-one;
rel-(4aR,8aR)-8,8-Difluoro-6-[3-[[2-fluoro-4-
(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-4a,5,7,8a-tetrahydro-4H-
15 pyrido[4,3-b][1,4]oxazin-3-one;
rel-(4aS,8aS)-8,8-Difluoro-6-[3-[4-(2,2,2-trifluoroethyl)phenyl]azetidine-1-
carbonyl]-4a,5,7,8a-tetrahydro-4H-pyrido[4,3-b][1,4]oxazin-3-one;
rel-(4aR,8aR)-8,8-Difluoro-6-[3-[4-(2,2,2-trifluoroethyl)phenyl]azetidine-1-
carbonyl]-4a,5,7,8a-tetrahydro-4H-pyrido[4,3-b][1,4]oxazin-3-one;
20 6-[4-[[4-(Trifluoromethyl)phenyl]methyl]piperidine-1-carbonyl]-4,5,7,8-
tetrahydropyrido[4,3-b][1,4]oxazin-3-one;
7-(4-Benzhydrylpiperidine-1-carbonyl)-1,5,6,8-tetrahydro-1,7-naphthyridin-2-one;
7-[3-[[2-Fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-1,5,6,8-
tetrahydro-1,7-naphthyridin-2-one;
25 rac-(4aS,8aS)-7-(4-Benzhydrylpiperidine-1-carbonyl)-1,3,4,4a,5,6,8,8a-octahydro-
1,7-naphthyridin-2-one;
rac-(4aS,8aS)-7-[3-[[2-Fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-
carbonyl]-1,3,4,4a,5,6,8,8a-octahydro-1,7-naphthyridin-2-one;
rac-(4aR,8aS)-6-[3-[[2-Fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-
30 carbonyl]-1,2,4,4a,5,7,8,8a-octahydropyrido[3,4-b]pyrazin-3-one;
(4aR,8aS)-or (4aS,8aR)-6-[3-[[2-Fluoro-4-
(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-1,2,4,4a,5,7,8,8a-
octahydropyrido[3,4-b]pyrazin-3-one;

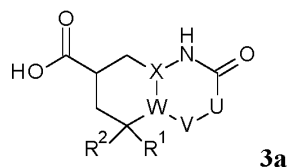
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- (4aS,8aR)- or (4aR,8aS)-6-[3-[[2-Fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-1,2,4,4a,5,7,8,8a-octahydropyrido[3,4-b]pyrazin-3-one; and
- 6-[3-[[2-Fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-1,2,4,5,7,8-hexahydropyrido[3,4-b]pyrazin-3-one.
21. A compound of formula (I) according to any one of claims 1 to 19, or a pharmaceutically acceptable salt thereof, selected from:
- (4aS,8aS)- or (4aR,8aR)-8,8-Difluoro-6-[3-[4-(2,2,2-trifluoroethyl)phenyl]azetidine-1-carbonyl]-4a,5,7,8a-tetrahydro-4H-pyrido[4,3-b][1,4]oxazin-3-one;
- rac-(4aR,8aR)-8,8-Difluoro-6-[3-[[2-fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-4a,5,7,8a-tetrahydro-4H-pyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8S,8aS)- or (4aR,8R,8aS)-6-[3-[[2-Fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-8-methyl-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 7-[3-[[2-Fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-1,5,6,8-tetrahydro-1,7-naphthyridin-2-one;
- rac-(4aR,8aS)-6-[3-[[2-Fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-1,2,4,4a,5,7,8,8a-octahydropyrido[3,4-b]pyrazin-3-one;
- (4aS,8aS)-6-[3-[[2-fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-4a-hydroxy-5,7,8,8a-tetrahydro-4H-pyrido[4,3-b][1,4]oxazin-3-one;
- rac-(4aS,8aS)-7-[3-[[2-fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-4-hydroxy-1,3,4,4a,5,6,8,8a-octahydro-1,7-naphthyridin-2-one; and
- 6-[3-[[2-fluoro-4-(trifluoromethyl)phenyl]methoxy]azetidine-1-carbonyl]-4,5,7,8-tetrahydropyrido[4,3-b][1,4]thiazin-3-one.
22. A process of manufacturing the compounds of formula (I) according to any one of claims 1 to 21, or pharmaceutically acceptable salts thereof, comprising:
- (a) reacting an amine of formula **2**, wherein m, n, Q, L, A, R³ and R⁴ are as defined in any one of claims 1 to 21,



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with a carboxylic acid **3a**, wherein U, V, W, X, R¹ and R² are as defined in any one of claim 1 to 21

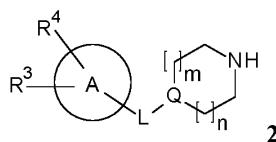


in the presence of a coupling reagent, and optionally in the presence of a base;

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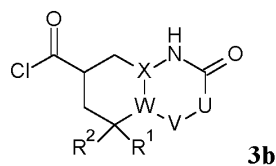
or

- (b) reacting an amine of formula **2**, wherein m, n, Q, L, A, R³ and R⁴ are as defined in any one of claims 1 to 21,



with a carboxylic acid chloride **3b**, wherein U, V, W, X, R¹ and R² are as defined in any one of claims 1 to 21

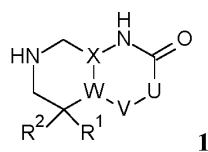
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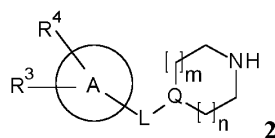
in the presence of a base; or

- (c) reacting a first amine of formula **1**, wherein U, V, W, X, R¹ and R² are as defined in any one of claims 1 to 21,

15



with a second amine **2**, wherein A, L, m, n, Q, R³ and R⁴ are as defined in any one of claims 1 to 21



in the presence of a base and a urea forming reagent,

20

to form said compound of formula (I).

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23. A compound of formula (I) according to any one of claims 1 to 21, or a pharmaceutically acceptable salt thereof, when manufactured according to the process of claim 22.
24. A compound of formula (I) according to any one of claims 1 to 21 and 23, or a pharmaceutically acceptable salt thereof, for use as therapeutically active substance.
25. A pharmaceutical composition comprising a compound of formula (I) according to any one of claims 1 to 21 and 23, or a pharmaceutically acceptable salt thereof, and a therapeutically inert carrier.
26. The use of a compound of formula (I) according to any one of claims 1 to 21 and 23, or a pharmaceutically acceptable salt thereof, or of a pharmaceutical composition according to claim 25 for the treatment or prophylaxis of neuroinflammation, neurodegenerative diseases, pain, cancer, mental disorders and/or inflammatory bowel disease in a mammal.
27. The use of a compound of formula (I) according to any one of claims 1 to 21 and 23, or a pharmaceutically acceptable salt thereof, or of a pharmaceutical composition according to claim 25 for the treatment or prophylaxis of multiple sclerosis, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, traumatic brain injury, neurotoxicity, stroke, epilepsy, anxiety, migraine, depression, hepatocellular carcinoma, colon carcinogenesis, ovarian cancer, neuropathic pain, chemotherapy induced neuropathy, acute pain, chronic pain, spasticity associated with pain, abdominal pain, abdominal pain associated with irritable bowel syndrome and/or visceral pain in a mammal.
28. A compound of formula (I) according to any one of claims 1 to 21 and 23, or a pharmaceutically acceptable salt thereof, or of a pharmaceutical composition according to claim 25 for use in the treatment or prophylaxis of neuroinflammation, neurodegenerative diseases, pain, cancer, mental disorders and/or inflammatory bowel disease in a mammal.
29. A compound of formula (I) according to any one of claims 1 to 21 and 23, or a pharmaceutically acceptable salt thereof, or of a pharmaceutical composition according to claim 25 for use in the treatment or prophylaxis of multiple sclerosis, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, traumatic

- brain injury, neurotoxicity, stroke, epilepsy, anxiety, migraine, depression, hepatocellular carcinoma, colon carcinogenesis, ovarian cancer, neuropathic pain, chemotherapy induced neuropathy, acute pain, chronic pain, spasticity associated with pain, abdominal pain, abdominal pain associated with irritable bowel syndrome and/or visceral pain in a mammal.
- 5
30. The use of a compound of formula (I) according to any one of claims 1 to 21 and 23, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for the treatment or prophylaxis of neuroinflammation, neurodegenerative diseases, pain, cancer, mental disorders and/or inflammatory bowel disease in a mammal.
- 10 31. The use of a compound of formula (I) according to any one of claims 1 to 21 and 23, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for the treatment or prophylaxis of multiple sclerosis, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, traumatic brain injury, neurotoxicity, stroke, epilepsy, anxiety, migraine, depression, hepatocellular carcinoma, colon
- 15 carcinogenesis, ovarian cancer, neuropathic pain, chemotherapy induced neuropathy, acute pain, chronic pain, spasticity associated with pain, abdominal pain, abdominal pain associated with irritable bowel syndrome and/or visceral pain in a mammal.
32. A method for the treatment or prophylaxis of neuroinflammation, neurodegenerative diseases, pain, cancer, mental disorders, and/or inflammatory bowel disease in a
- 20 mammal, which method comprises administering an effective amount of a compound of formula (I) according to any one of claims 1 to 21 and 23, or a pharmaceutically acceptable salt thereof, or of a pharmaceutical composition according to claim 25 to the mammal.
33. A method for the treatment or prophylaxis of multiple sclerosis, Alzheimer's disease,
- 25 Parkinson's disease, amyotrophic lateral sclerosis, traumatic brain injury, neurotoxicity, stroke, epilepsy, anxiety, migraine, depression, hepatocellular carcinoma, colon carcinogenesis, ovarian cancer, neuropathic pain, chemotherapy induced neuropathy, acute pain, chronic pain, spasticity associated with pain in a mammal, abdominal pain, abdominal pain associated with irritable bowel syndrome
- 30 and/or visceral pain which method comprises administering an effective amount of a compound of formula (I) according to any one of claims 1 to 21 and 23, or a

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pharmaceutically acceptable salt thereof, or of a pharmaceutical composition according to claim 25 to the mammal.

34. The invention as described hereinbefore.