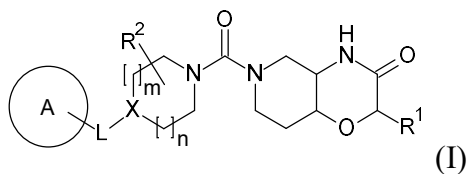


activation of MAGL is a promising new therapeutic strategy for providing neuroprotection and myelin regeneration. Accordingly, there is a high unmet medical need for new MAGL inhibitors.

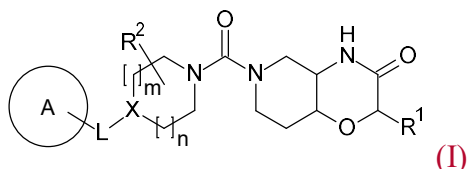
Summary of the Invention

In a first aspect, the present invention provides a compound of formula (I)



wherein A, L, X, m, n, R¹ and R² are as described herein.

In a first aspect, the present disclosure provides a compound of formula (I)



or a pharmaceutically acceptable salt thereof,

wherein:

X is C-R³; m is 0 or 1; n is selected from 0, 1 and 2; and L is selected from -C≡C-, -CHR⁴-NR⁵-CH₂-, -NR⁵-CH₂-CHR⁴-, -NR⁵-CHR⁴-CH₂-, -CH₂-NR⁵-CHR⁴-, -(CR⁶R⁷)_p-C(O)-NR⁸-, -C(O)-NR⁸-(CR⁶R⁷)_p-, -(CR⁶R⁷)_p-NR⁸-C(O)-, -NR⁸-C(O)-(CR⁶R⁷)_p-, -(CH₂)_qNR⁹-, -NR⁹-(CH₂)_q-, -S-, -S(O)-, -SO₂-, -SCH₂-, -CH₂S-, -S(O)CH₂-, -CH₂S(O)-, -SO₂CH₂-, and -CH₂SO₂-; or

X is N; m is 1; n is 1 or 2; and L is selected from -NR⁵-CH₂-CHR⁴-, -NR⁵-CHR⁴-CH₂-, and -NR⁸-C(O)-(CR⁶R⁷)_p-;

p and q are each independently selected from 0, 1 and 2;

A is selected from:

(i) C₆-C₁₄-aryl substituted with R¹⁰, R¹¹ and R¹²;

(ii) 5- to 14-membered heteroaryl substituted with R¹³, R¹⁴ and R¹⁵; and

(iii) 3- to 14-membered heterocycloalkyl substituted with R¹⁶, R¹⁷ and R¹⁸;

(iv) C₃-C₁₀-cycloalkyl substituted with R²²;

R¹ is hydrogen or C₁₋₆-alkyl;

R² is selected from hydrogen, C₁₋₆-alkyl and hydroxy-C₁₋₆-alkyl;

R³ is selected from hydrogen, halogen, hydroxy, C₁₋₆-alkoxy, C₁₋₆-alkyl and halo-C₁₋₆-alkyl;

5 R⁴ is selected from hydrogen, C₁₋₆-alkyl and halo-C₁₋₆-alkyl;

R⁵ is selected from hydrogen, C₁₋₆-alkyl and halo-C₁₋₆-alkyl-CH₂-;

each of R⁶ and R⁷ is independently hydrogen or C₁₋₆-alkyl; or

R⁶ and R⁷, taken together with the carbon atom to which they are attached, form a 3- to 14-membered heterocycloalkyl or a C₃₋₁₀-cycloalkyl;

10 R⁸ is selected from hydrogen, C₁₋₆-alkyl, and hydroxy-C₁₋₆-alkyl;

R⁹ is selected from hydrogen, C₁₋₆-alkyl, halo-C₁₋₆-alkyl-CH₂-, (C₁₋₆-alkyl)(halo-C₁₋₆-alkyl)CH- and hydroxy-C₁₋₆-alkyl-CH₂-;

each of R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷ and R¹⁸ is independently selected from hydrogen, halogen, cyano, hydroxy, C₁₋₆-alkyl, halo-C₁₋₆-alkyl, hydroxy-C₁₋₆-alkyl, halo-C₁₋₆-alkyl-

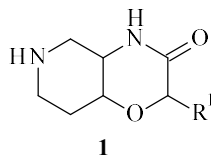
15 CH(OH)-, C₁₋₆-alkoxy, C₁₋₆-alkoxy-C₁₋₆-alkyl, halo-C₁₋₆-alkoxy, SF₅, C₁₋₆-alkylsulfonyl, C₃₋₁₀-cycloalkyl, C₃₋₁₀-cycloalkyl substituted with R¹⁹, 3- to 14-membered heterocycloalkyl, 3- to 14-membered heterocycloalkyl substituted with R²⁰, 5- to 14-membered heteroaryl, C₆-C₁₄-aryl and halo-C₆-C₁₄-aryl;

each of R¹⁹ and R²⁰ is independently selected from C₁₋₆-alkyl, cyano, and hydroxy; and

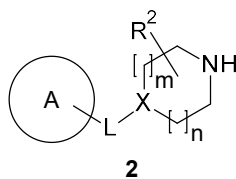
20 R²² is hydrogen or hydroxy.

In one aspect, the present invention disclosure provides a process of manufacturing the urea compounds of formula (I) described herein, comprising:

reacting a first amine of formula **1**, wherein R¹ is as described herein, preferably wherein R¹ is hydrogen,



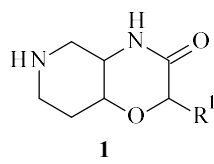
with a second amine **2**, wherein A, L, m, n, X and R² are as described herein



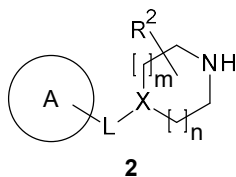
in the presence of a base and a urea forming reagent,
to form said compound of formula (I).

- 5 In another aspect, the present disclosure provides a process of manufacturing the compounds of formula (I) as described herein, comprising:

reacting a first amine of formula 1, wherein R¹ is as described herein,



with a second amine **2**, wherein A, L, m, n, X and R² are as described herein



in the presence of a base and a urea forming reagent,
to form said compound of formula (I).

In a further aspect, the present invention-disclosure provides a compound of formula (I) as described herein, when manufactured according to the processes described herein.

- 15 In a further aspect, the present invention-disclosure provides a compound of formula (I) as described herein, for use as therapeutically active substance.

In a further aspect, the present invention-disclosure provides a pharmaceutical composition comprising a compound of formula (I) as described herein and a therapeutically inert carrier.

~~In a further aspect, the~~ The present ~~invention disclosure~~ provides the use of a compound of formula (I) as described herein or of a pharmaceutical composition described herein for inhibiting monoacylglycerol lipase (MAGL) in a mammal.

~~In a further aspect, the~~ The present ~~invention disclosure~~ provides the use of a compound of formula (I) as described herein or of a pharmaceutical composition described herein for the treatment or prophylaxis of neuroinflammation, neurodegenerative diseases, pain, cancer and/or mental disorders in a mammal.

~~In a further aspect, the~~ The present ~~invention disclosure~~ provides the use of a compound of formula (I) as described herein or of a pharmaceutical composition described herein 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 and/or spasticity associated with pain in a mammal.

~~In a further aspect, the~~ The present ~~invention disclosure~~ provides a compound of formula (I) as described herein or a pharmaceutical composition described herein for use in a method of inhibiting monoacylglycerol lipase in a mammal.

In a further aspect, the present ~~invention disclosure~~ provides a compound of formula (I) as described herein or a pharmaceutical composition described herein for use in the treatment or prophylaxis of neuroinflammation, neurodegenerative diseases, pain, cancer and/or mental disorders in a mammal.

In a further aspect, the present ~~invention disclosure~~ provides a compound of formula (I) as described herein or a pharmaceutical composition described herein, 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 and/or spasticity associated with pain in a mammal.

~~In a further aspect,~~ The present ~~invention~~ disclosure provides the use of a compound of formula (I) as described herein for the preparation of a medicament for inhibiting monoacylglycerol lipase in a mammal.

~~In a further aspect, the~~ present ~~invention~~ disclosure provides the use of a compound of formula (I) as described herein for the preparation of a medicament for the treatment or prophylaxis of neuroinflammation, neurodegenerative diseases, pain, cancer and/or mental disorders in a mammal.

In another aspect, the present disclosure provides the use of a compound of formula (I) as described herein or a pharmaceutical composition as described herein in the preparation of a medicament for the treatment or prophylaxis of neuroinflammation, neurodegenerative diseases, pain, cancer and/or mental disorders in a mammal.

~~In a further aspect, the~~ present ~~invention~~ disclosure provides the use of a compound of formula (I) as described herein 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 carcinogenesis, ovarian cancer, neuropathic pain, chemotherapy induced neuropathy, acute pain, chronic pain and/or spasticity associated with pain in a mammal.

In another aspect, the present disclosure provides the use of a compound of formula (I) as described herein or a pharmaceutical composition as described herein in 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 carcinogenesis, ovarian cancer, neuropathic pain, chemotherapy induced neuropathy, acute pain, chronic pain and/or spasticity associated with pain in a mammal.

~~In a further aspect, the~~ present ~~invention~~ disclosure provides a method for inhibiting monoacylglycerol lipase in a mammal, which method comprises administering an effective amount of a compound of formula (I) as described herein or of a pharmaceutical composition described herein to the mammal.

~~In a further aspect, the~~ present ~~invention~~ disclosure provides a method for the treatment or prophylaxis of neuroinflammation, neurodegenerative diseases, pain, cancer and/or mental disorders in a mammal, which method comprises administering an effective amount of a

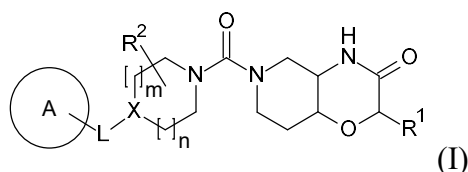
compound of formula (I) as described herein or of a pharmaceutical composition described herein to the mammal.

~~In a further aspect, the~~ The present ~~invention disclosure~~ provides a method 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 and/or spasticity associated with pain in a mammal, which method comprises administering an effective amount of a compound of formula (I) as described herein or of a pharmaceutical composition described herein to the mammal.

~~In one aspect, the~~ The present ~~invention disclosure~~ also provides a method for determining the MAGL inhibitory activity of a test compound, e.g. of a compound of formula (I) described herein, comprising measuring the ratio of arachidonic acid / d8-arachidonic acid in a solution.

CLAIMS

1. A compound of formula (I)



or a pharmaceutically acceptable salt thereof,

wherein:

X is C-R³; m is 0 or 1; n is selected from 0, 1 and 2; and L is selected from -C≡C-, -CHR⁴-NR⁵-CH₂-, -NR⁵-CH₂-CHR⁴-, -NR⁵-CHR⁴-CH₂-, -CH₂-NR⁵-CHR⁴-, -(CR⁶R⁷)_p-C(O)-NR⁸-, -C(O)-NR⁸-(CR⁶R⁷)_p-, -(CR⁶R⁷)_p-NR⁸-C(O)-, -NR⁸-C(O)-(CR⁶R⁷)_p-, -(CH₂)_qNR⁹-, -NR⁹-(CH₂)_q-, -S-, -S(O)-, -SO₂-, -SCH₂-, -CH₂S-, -S(O)CH₂-, -CH₂S(O)-, -SO₂CH₂-, and -CH₂SO₂-; or

X is N; m is 1; n is 1 or 2; and L is selected from -NR⁵-CH₂-CHR⁴-, -NR⁵-CHR⁴-CH₂-, and -NR⁸-C(O)-(CR⁶R⁷)_p-;

p and q are each independently selected from 0, 1 and 2;

A is selected from:

- (i) C₆-C₁₄-aryl substituted with R¹⁰, R¹¹ and R¹²;
- (ii) 5- to 14-membered heteroaryl substituted with R¹³, R¹⁴ and R¹⁵; and
- (iii) 3- to 14-membered heterocycloalkyl substituted with R¹⁶, R¹⁷ and R¹⁸;
- (iv) C₃-C₁₀-cycloalkyl substituted with R²², ~~R²³~~, and ~~R²⁴~~;

R¹ is hydrogen or C₁₋₆-alkyl;

R² is selected from hydrogen, C₁₋₆-alkyl and hydroxy-C₁₋₆-alkyl;

R³ is selected from hydrogen, halogen, hydroxy, C₁₋₆-alkoxy, C₁₋₆-alkyl and halo-C₁₋₆-alkyl;

R⁴ is selected from hydrogen, C₁₋₆-alkyl and halo-C₁₋₆-alkyl;

R⁵ is selected from hydrogen, C₁₋₆-alkyl and halo-C₁₋₆-alkyl-CH₂-;

each of R⁶ and R⁷ is independently hydrogen or C₁₋₆-alkyl; or

R⁶ and R⁷, taken together with the carbon atom to which they are attached, form a 3- to 14-membered heterocycloalkyl or a C₃₋₁₀-cycloalkyl;

R⁸ is selected from hydrogen, C₁₋₆-alkyl, and hydroxy-C₁₋₆-alkyl;

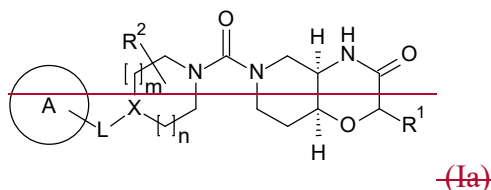
R⁹ is selected from hydrogen, C₁₋₆-alkyl, halo-C₁₋₆-alkyl-CH₂-, (C₁₋₆-alkyl)(halo-C₁₋₆-alkyl)CH- and hydroxy-C₁₋₆-alkyl-CH₂-;

each of R^{10} , R^{11} , R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} and R^{18} is independently selected from hydrogen, halogen, cyano, hydroxy, C_{1-6} -alkyl, halo- C_{1-6} -alkyl, hydroxy- C_{1-6} -alkyl, halo- C_{1-6} -alkyl-CH(OH)-, C_{1-6} -alkoxy, C_{1-6} -alkoxy- C_{1-6} -alkyl, halo- C_{1-6} -alkoxy, SF_5 , C_{1-6} -alkylsulfonyl, C_{3-10} -cycloalkyl, C_{3-10} -cycloalkyl substituted with R^{19} , 3- to 14-membered heterocycloalkyl, 3- to 14-membered heterocycloalkyl substituted with R^{20} , 5- to 14-membered heteroaryl, C_6 - C_{14} -aryl and halo- C_6 - C_{14} -aryl; ~~and~~

each of R^{19} and R^{20} is independently selected from C_{1-6} -alkyl, cyano, and hydroxy; and

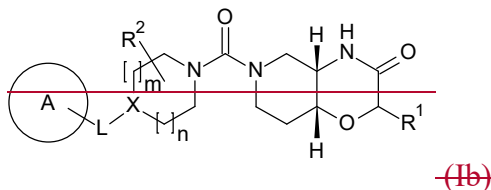
R^{22} is hydrogen or hydroxy.

~~2. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound of formula (I) is a compound of formula (Ia):~~



~~wherein A, L, X, m, n, R^1 and R^2 are as defined in claim 1.~~

~~3. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound of formula (I) is a compound of formula (Ib):~~



~~wherein A, L, X, m, n, R^1 and R^2 are as defined in claim 1.~~

4.2. The compound of formula I according to any one of claims 1-~~23~~, or a pharmaceutically acceptable salt thereof, wherein:

X is $C-R^3$;

m, n and ~~pn~~ are each independently 0 or 1; ~~and~~

L is selected from $-C\equiv C-$, $-CHR^4-NR^5-CH_2-$, $-CH_2-NR^5-CHR^4-$, $-(CR^6R^7)_p-C(O)-NR^8-$, $-(CR^6R^7)_p-NR^8-C(O)-$, $-(CH_2)_qNR^9-$, $-S-$, $-S(O)-$, $-SO_2-$, $-SCH_2-$, $-CH_2S-$, $-S(O)CH_2-$, $-CH_2S(O)-$, $-SO_2CH_2-$, and $-CH_2SO_2-$; ~~and~~

q is 0;

R² is hydrogen;

R³ is selected from hydrogen, hydroxy, and C₁₋₆-alkyl;

R⁴ is halo-C₁₋₆-alkyl;

R⁶ and R⁷ are both hydrogen; or

5 R⁶ and R⁷, together with the carbon atom to which they are attached, form a C₃₋₁₀-
cycloalkyl; and

R⁹ is C₁₋₆-alkyl.

~~5.3.~~ The compound of formula I according to claim 2~~any one of claims 1-4~~, or a
pharmaceutically acceptable salt thereof, wherein:

10 X is C-R³;

m and n are both 0; or

m and n are both 1; ~~and~~

q is 0;

L is selected from -C≡C-, -CHR⁴-NR⁵-CH₂-, -(CH₂)_qNR⁹-, -SCH₂-, and -CH₂S-

15 R², R³ and R⁵ are all hydrogen;

R⁴ is halo-C₁₋₆-alkyl; and

R⁹ is C₁₋₆-alkyl.

4. The compound of formula I according to claim 3, or a pharmaceutically acceptable
salt thereof, wherein:

20 X is C-R³;

m and n are both 0; or

m and n are both 1;

q is 0;

L is selected from -C≡C-, -CHR⁴-NR⁵-CH₂-, -(CH₂)_qNR⁹-, -SCH₂-, and -CH₂S-

25 R², R³ and R⁵ are all hydrogen;

R⁴ is CF₃; and

R⁹ is methyl.

~~6. The compound of formula I according to any one of claims 1-5, or a
pharmaceutically acceptable salt thereof, wherein p is 0 or 1.~~

30 ~~7. The compound of formula I according to any one of claims 1-6, or a
pharmaceutically acceptable salt thereof, wherein q is 0.~~

8.5. The compound of formula I according to any one of claims 1-~~74~~, or a pharmaceutically acceptable salt thereof, wherein A is selected from:

- (i) C₆-C₁₄-aryl substituted with R¹⁰, R¹¹ and R¹²;
- (ii) 5- to 14-membered heteroaryl substituted with R¹³, R¹⁴ and R¹⁵; and
- (iii) C₃-C₁₀-cycloalkyl substituted with R²², ~~R²³~~, and ~~R²⁴~~.

wherein:

R¹⁰ is selected from hydrogen, C₁₋₆-alkyl, C₁₋₆-alkylsulfonyl, C₁₋₆-alkoxy, halo-C₁₋₆-alkyl, halo-C₁₋₆-alkoxy, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₃₋₁₀-cycloalkyl substituted with R¹⁹, cyano, and halogen;

R¹¹ is selected from hydrogen, C₁₋₆-alkyl, and halogen;

R¹² is hydrogen or halogen;

R¹³ is halogen;

R¹⁴ and R¹⁵ are both hydrogen;

R¹⁹ is hydroxy or cyano; and

R²² is hydrogen or hydroxy.

9.6. The compound of formula I according to any one of claims 1-~~74~~, or a pharmaceutically acceptable salt thereof, wherein:

A is C₆-C₁₄-aryl substituted with R¹⁰, R¹¹ and R¹²;

R¹⁰ is selected from C₁₋₆-alkyl, halo-C₁₋₆-alkyl, halo-C₁₋₆-alkoxy, C₃₋₁₀-cycloalkyl, and halogen;

R¹¹ is selected from hydrogen, C₁₋₆-alkyl, and halogen; and

R¹² is hydrogen or halogen.

10.7. The compound of formula I according to any one of claims 1-~~74~~, or a pharmaceutically acceptable salt thereof, wherein:

A is phenyl substituted with R¹⁰, R¹¹ and R¹²;

R¹⁰ is methyl, difluoromethyl, CF₃, OCF₃, cyclopropyl, fluoro, or chloro;

R¹¹ is hydrogen, methyl, chloro, or fluoro; and

R¹² is hydrogen or fluoro.

11.8. The compound of formula I according to any one of claims 1-~~107~~, or a pharmaceutically acceptable salt thereof, wherein R¹ is hydrogen.

- ~~12.—The compound of formula I according to any one of claims 1–11, or a pharmaceutically acceptable salt thereof, wherein R² is hydrogen.~~
- ~~13.—The compound of formula I according to any one of claims 1–12, or a pharmaceutically acceptable salt thereof, wherein R³ is hydrogen, hydroxy, or C₁₋₆-alkyl.~~
- 5 ~~14.—The compound of formula I according to any one of claims 1–12, or a pharmaceutically acceptable salt thereof, wherein R³ is hydrogen.~~
- ~~15.—The compound of formula I according to any one of claims 1–14, or a pharmaceutically acceptable salt thereof, wherein R⁴ is halo-C₁₋₆-alkyl.~~
- 10 ~~16.—The compound of formula I according to any one of claims 1–14, or a pharmaceutically acceptable salt thereof, wherein R⁴ is CF₃.~~
- ~~17.—The compound of formula I according to any one of claims 1–16, or a pharmaceutically acceptable salt thereof, wherein R⁵ is hydrogen.~~
- ~~18.—The compound of formula I according to any one of claims 1–17, or a pharmaceutically acceptable salt thereof, wherein R⁶ and R⁷ are both hydrogen; or R⁶ and R⁷, together with the carbon atom to which they are attached, form a C₃₋₁₀-cycloalkyl.~~
- 15 ~~19.—The compound of formula I according to any one of claims 1–18, or a pharmaceutically acceptable salt thereof, wherein R⁹ is C₁₋₆-alkyl.~~
- 20 ~~20.—The compound of formula I according to any one of claims 1–18, or a pharmaceutically acceptable salt thereof, wherein R⁹ is methyl.~~
- ~~21.—The compound of formula I according to any one of claims 1–20, or a pharmaceutically acceptable salt thereof, wherein R¹⁰ is hydrogen, C₁₋₆-alkyl, C₁₋₆-alkylsulfonyl, C₁₋₆-alkoxy, halo-C₁₋₆-alkyl, halo-C₁₋₆-alkoxy, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₃₋₁₀-cycloalkyl substituted with R¹⁹, cyano, or halogen.~~
- 25 ~~22.—The compound of formula I according to any one of claims 1–20, or a pharmaceutically acceptable salt thereof, wherein R¹⁰ is C₁₋₆-alkyl, halo-C₁₋₆-alkyl, halo-C₁₋₆-alkoxy, C₃₋₁₀-cycloalkyl, or halogen.~~

23. ~~The compound of formula I according to any one of claims 1-20, or a pharmaceutically acceptable salt thereof, wherein R¹⁰ is methyl, difluoromethyl, CF₃, OCF₃, cyclopropyl, fluoro, or chloro.~~
- 5 24. ~~The compound of formula I according to any one of claims 1-23, or a pharmaceutically acceptable salt thereof, wherein R¹¹ is hydrogen, C₁₋₆-alkyl, or halogen.~~
25. ~~The compound of formula I according to any one of claims 1-23, or a pharmaceutically acceptable salt thereof, wherein R¹¹ is hydrogen, methyl, chloro, or fluoro.~~
- 10 26. ~~The compound of formula I according to any one of claims 1-25, or a pharmaceutically acceptable salt thereof, wherein R¹² is hydrogen or halogen.~~
27. ~~The compound of formula I according to any one of claims 1-25, or a pharmaceutically acceptable salt thereof, wherein R¹² is hydrogen or fluoro.~~
28. ~~The compound of formula I according to any one of claims 1-27, or a pharmaceutically acceptable salt thereof, wherein R¹³ is halogen.~~
- 15 29. ~~The compound of formula I according to any one of claims 1-28, or a pharmaceutically acceptable salt thereof, wherein R¹⁴ is hydrogen.~~
30. ~~The compound of formula I according to any one of claims 1-29, or a pharmaceutically acceptable salt thereof, wherein R¹⁵ is hydrogen.~~
- 20 31. ~~The compound of formula I according to any one of claims 1-30, or a pharmaceutically acceptable salt thereof, wherein R¹⁹ is hydroxy or cyano.~~
32. ~~The compound of formula I according to any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein R²² is hydrogen or hydroxy.~~
33. ~~The compound of formula I according to any one of claims 1-32, or a pharmaceutically acceptable salt thereof, wherein R²³ is hydrogen.~~
- 25 34. ~~The compound of formula I according to any one of claims 1-33, or a pharmaceutically acceptable salt thereof, wherein R²⁴ is hydrogen.~~

35. ~~The compound of formula I according to any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein:~~

~~X is C-R³;~~

~~L is selected from C≡C-, CHR⁴-NR⁵-CH₂-, CH₂-NR⁵-CHR⁴-, (CR⁶R⁷)_p-C(O)-NR⁸-, (CR⁶R⁷)_p-NR⁸-C(O)-, (CH₂)_qNR⁹-, S-, S(O)-, SO₂-, SCH₂-, CH₂S-, S(O)CH₂-, CH₂S(O)-, and SO₂CH₂-;~~

~~m, n and p are each independently 0 or 1;~~

~~q is 0;~~

~~A is selected from:~~

- ~~(i) C₆-C₁₄-aryl substituted with R¹⁰, R¹¹ and R¹²;~~
~~(ii) 5- to 14-heteroaryl substituted with R¹³, R¹⁴ and R¹⁵; and~~
~~(iii) C₃-C₁₀-cycloalkyl substituted with R²², R²³, and R²⁴;~~

~~R¹ and R² are both hydrogen;~~

~~R³ is selected from hydrogen, hydroxy, and C₁₋₆-alkyl;~~

~~R⁴ is halo-C₁₋₆-alkyl;~~

~~R⁵ is hydrogen or C₁₋₆-alkyl;~~

~~R⁶ and R⁷ are both hydrogen; or~~

~~R⁶ and R⁷, together with the carbon atom to which they are attached, form a C₃₋₁₀-cycloalkyl;~~

~~R⁸ is selected from hydrogen, C₁₋₆-alkyl and hydroxy-C₁₋₆-alkyl;~~

~~R⁹ is C₁₋₆-alkyl;~~

~~R¹⁰ is selected from hydrogen, C₁₋₆-alkyl, C₁₋₆-alkylsulfonyl, C₁₋₆-alkoxy, C₁₋₆-alkoxy-C₁₋₆-alkyl, halo-C₁₋₆-alkyl, halo-C₁₋₆-alkoxy, C₃₋₁₀-cycloalkyl, C₃₋₁₀-cycloalkyl substituted with R¹⁹, cyano, and halogen;~~

~~R¹¹ is selected from hydrogen, C₁₋₆-alkyl, and halogen;~~

~~R¹² is hydrogen or halogen;~~

~~R¹³ is halogen;~~

~~R¹⁴ and R¹⁵ are both hydrogen;~~

~~R¹⁹ is hydroxy or cyano;~~

~~R²² is hydrogen or hydroxy; and~~

~~R²³ and R²⁴ are both hydrogen.~~

36. ~~The compound of formula I according to any one of claims 1-3, wherein:~~

X is $C-R^3$;

L is selected from $C\equiv C$, $CHR^4-NR^5-CH_2$, $(CH_2)_qNR^9$, SCH_2 , and CH_2S ;

m and n are both 0; or

5 m and n are both 1;

q is 0;

A is C_6-C_{14} -aryl substituted with R^{10} , R^{11} and R^{12} ;

R^1 , R^2 and R^3 are all hydrogen;

R^4 is halo- C_{1-6} -alkyl;

10 R^5 is hydrogen;

R^9 is C_{1-6} -alkyl;

R^{10} is selected from C_{1-6} -alkyl, halo- C_{1-6} -alkyl, halo- C_{1-6} -alkoxy, C_{3-10} -cycloalkyl, and halogen;

R^{11} is selected from hydrogen, C_{1-6} -alkyl, and halogen; and

15 R^{12} is hydrogen or halogen.

37. The compound of formula I according to any one of claims 1-3, wherein:

X is $C-R^3$;

L is selected from $C\equiv C$, $CHR^4-NR^5-CH_2$, $(CH_2)_qNR^9$, SCH_2 , and CH_2S ;

m and n are both 0; or

20 m and n are both 1;

q is 0;

A is phenyl substituted with R^{10} , R^{11} and R^{12} ;

R^1 , R^2 and R^3 are all hydrogen;

25 R^4 is CF_3 ;

R^5 is hydrogen;

R^9 is methyl;

R^{10} is selected from methyl, difluoromethyl, CF_3 , OCF_3 , cyclopropyl, chloro, and fluoro;

30 R^{11} is selected from hydrogen, methyl, chloro, and fluoro; and

R^{12} is hydrogen or fluoro.

38.9. A compound of formula (I) according to any one of claims 1 to 378, selected from the compounds disclosed in Table 1;

- (4aR,8aS)-6-(3-((2-Chloro-4-(trifluoromethyl)phenyl)thio)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(3-((2-Chloro-4-(trifluoromethyl)phenyl)sulfonyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 5 (4aR,8aS)-6-(3-((2-Chloro-4-(trifluoromethyl)phenyl)sulfinyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(3-((2-Chloro-4-(trifluoromethyl)phenyl)sulfinyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(3-(((2-Chloro-4-(trifluoromethyl)phenyl)thio)methyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 10 (4aR,8aS)-6-(3-((2-Fluoro-6-(trifluoromethyl)benzyl)sulfonyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-[3-[[2-Fluoro-6-(trifluoromethyl)phenyl]methylsulfinyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 15 (4aR,8aS)-6-(3-(((2-Chloro-4-(trifluoromethyl)phenyl)sulfonyl)methyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(3-(((2-Chloro-4-(trifluoromethyl)phenyl)sulfinyl)methyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(3-((2-Fluoro-4-(trifluoromethyl)benzyl)thio)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 20 (4aR,8aS)-6-(3-((2,6-Dichlorophenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-[3-[2-[2-Fluoro-4-(trifluoromethyl)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 25 (4aR,8aS)-6-(3-((2,6-Difluorophenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(3-((3-Chloro-4-(trifluoromethyl)phenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(3-((2-Chloro-6-fluorophenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 30 (4aR,8aS)-6-(3-((2-Chloro-4-cyclopropylphenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(3-((2-Methoxyphenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;

- (4aR,8aS)-6-[3-[2-[4-Chloro-2-(trifluoromethyl)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-(3-Chlorophenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 5 (4aR,8aS)-6-[3-[2-[4-Trifluoromethoxy]phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-[4-(Trifluoromethyl)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-(3-Fluoro-2-methylphenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 10 (4aR,8aS)-6-[3-[2-(2,6-Dimethylphenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-[2-(Trifluoromethoxy)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 15 (4aR,8aS)-6-[3-[2-(2-Bromophenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-(3-((2-Chloro-3-fluorophenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(3-(o-Tolyethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 20 (4aR,8aS)-6-[3-[2-(4-Chloro-2-fluorophenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-[2-(Difluoromethoxy)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 25 2-[2-[1-[(4aR,8aS)-3-Oxo-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazine-6-carbonyl]azetidin-3-yl]ethynyl]-3-chlorobenzonitrile;
- (4aR,8aS)-6-[3-[2-[4-(Difluoromethoxy)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 1-[4-[2-[1-[(4aR,8aS)-3-Oxo-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazine-6-carbonyl]azetidin-3-yl]ethynyl]phenyl]cyclopropane-1-carbonitrile;
- 30 (4aR,8aS)-6-[3-[2-(4-Cyclopropylphenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-[4-(1-Hydroxycyclopropyl)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;

- (4aR,8aS)-6-[3-[2-(3-Methoxyphenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-[2-(Difluoromethyl)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 5 (4aR,8aS)-6-[3-[2-(3-Methoxy-2-methylphenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-(2-Chloro-6-methylphenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-(2-Chloro-5-fluorophenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 10 (4aR,8aS)-6-[3-[2-(4-Methylsulfonylphenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-(5-Chlorothiophen-2-yl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 15 (4aR,8aS)-6-[3-[2-(5-Chlorothiophen-3-yl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-[2-Chloro-6-fluoro-4-(trifluoromethyl)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-(2-Chlorophenyl)ethynyl]-3-hydroxyazetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 20 (4aR,8aS)-6-[3-[2-[2-(Methoxymethyl)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-(4-((2-(Trifluoromethyl)phenyl)ethynyl)piperidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 25 (4aR,8aS)-6-(4-((2-Methoxyphenyl)ethynyl)piperidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(4-(o-Tolyethynyl)piperidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(4-((2,6-Dimethylphenyl)ethynyl)piperidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 30 (4aR,8aS)-6-(4-((2,4-Dichlorophenyl)ethynyl)-4-methylpiperidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(4-((2-Chloro-4-fluorophenyl)ethynyl)-4-methylpiperidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;

- (4aR,8aS)-6-[3-[2-(1-Hydroxycyclopentyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- (4aR,8aS)-6-[3-[2-(Cyclopenten-1-yl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 5 (4aR,8aS)-6-(3-((2-Chloro-4-(trifluoromethyl)phenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (4aR,8aS)-6-(3-((2-Fluoro-6-(trifluoromethyl)benzyl)thio)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (+)- or (-)-(4aR,8aS)-6-[3-[[[2,2,2-Trifluoro-1-[4-(trifluoromethyl)phenyl]ethyl]amino]methyl]azetidine-1-carbonyl]hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 10 (+)- or (-)-N-Benzyl-N-(2-hydroxyethyl)-1-((4aR,8aS)-3-oxooctahydro-2H-pyrido[4,3-b][1,4]oxazine-6-carbonyl)piperidine-4-carboxamide;
- (+)- or (-)-N-Benzyl-1-((4aR,8aS)-3-oxooctahydro-2H-pyrido[4,3-b][1,4]oxazine-6-carbonyl)piperidine-4-carboxamide;
- 15 (+)- or (-)-(4aR,8aS)-6-(3-(((2,2,2-Trifluoro-1-(3-(trifluoromethyl)phenyl)ethyl)amino)methyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (+)- or (-)-(4aR,8aS)-6-(3-(((1-(2,4-Dichlorophenyl)-2,2,2-trifluoroethyl)amino)methyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 20 (+)- or (-)-(4aR,8aS)-6-(3-(((1-(2-Chlorophenyl)-2,2,2-trifluoroethyl)amino)methyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- (+)- or (-)-(4aR,8aS)-6-(3-(((2,2,2-Trifluoro-1-phenylethyl)amino)methyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 25 (+)- or (-)-2-Chloro-4-fluoro-N-(1-((4aR,8aS)-3-oxooctahydro-2H-pyrido[4,3-b][1,4]oxazine-6-carbonyl)azetidin-3-yl)benzamide;
- (+)- or (-)-(4aR,8aS)-6-(3-((Methyl(2,2,2-trifluoro-1-(4-(trifluoromethyl)phenyl)ethyl)amino)methyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 30 N-[1-[(4aR,8aS)-3-oxo-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazine-6-carbonyl]piperidin-4-yl]-N-methyl-1-[3-(trifluoromethyl)phenyl]cyclopropane-1-carboxamide;

- N-[1-[(4aR,8aS)-3-oxo-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazine-6-carbonyl]piperidin-4-yl]-2-[2-chloro-3-(trifluoromethyl)phenyl]-N-methylacetamide;
- 5 N-[1-[(4aR,8aS)-3-oxo-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazine-6-carbonyl]piperidin-4-yl]-2-[2-chloro-5-(trifluoromethyl)phenyl]-N-methylacetamide;
- N-[1-[(4aR,8aS)-3-oxo-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazine-6-carbonyl]piperidin-4-yl]-N-methyl-4-(trifluoromethyl)benzamide;
- 10 N-[1-[(4aR,8aS)-3-oxo-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazine-6-carbonyl]piperidin-4-yl]-N-methyl-2-[3-(trifluoromethyl)phenyl]acetamide;
(4aR,8aS)-6-[3-[[[2,2,2-Trifluoro-1-(4-fluorophenyl)ethyl]amino]methyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
(4aR,8aS)-6-[4-[2,2,2-Trifluoro-1-[[3-(trifluoromethyl)phenyl]methylamino]ethyl]piperidine-1-carbonyl]-4,4a,5,7,8,8a-
- 15 hexahydropyrido[4,3-b][1,4]oxazin-3-one;
(4aR,8aS)-6-[4-[2-(2-Chlorophenyl)ethynyl]piperidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
(4aR,8aS)-6-[4-[2-(4-Chloropyridin-3-yl)ethynyl]piperidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
- 20 (+)- or (-)-(4aR,8aS)-6-[4-[2-(3-Chloropyridin-2-yl)ethynyl]piperidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
(+)- or (-)-(4aR,8aS)-6-[4-[2-(2-Chloro-4-fluorophenyl)ethynyl]piperidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
(+)- or (-)-(4aR,8aS)-6-(4-((3-Chlorophenyl)ethynyl)piperidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 25 (+)- or (-)-(4aR,8aS)-6-(4-((4-Chlorophenyl)ethynyl)piperidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
(+)- or (-)-(4aR,8aS)-6-(4-((2,4-Dichlorophenyl)ethynyl)piperidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
- 30 (+)- or (-)-(4aR,8aS)-6-[4-[2-(2-Chlorophenyl)ethynyl]-4-hydroxypiperidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
(4aR,8aS)-6-[3-[2-(2-Chlorophenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;

(4aR,8aS)-6-(3-((2,4-Dichlorophenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;

(4aR,8aS)-6-[3-[2-(2-Chloro-4-fluorophenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;

5 (4aR,8aS)-6-[4-[N-methyl-4-(trifluoromethyl)anilino]piperidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one; and

(4aR,8aS)-6-[3-[N-methyl-4-(trifluoromethyl)anilino]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one.

39.10. A compound of formula (I) according to any

10 one of claims 1 to 378, selected from:

(+)- or (-)-(4aR,8aS)-6-[3-[[[2,2,2-Trifluoro-1-[4-(trifluoromethyl)phenyl]ethyl]amino]methyl]azetidine-1-carbonyl]hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;

15 (4aR,8aS)-6-[4-[2-(2-Chlorophenyl)ethynyl]piperidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;

(+)- or (-)-(4aR,8aS)-6-[4-[2-(2-Chloro-4-fluorophenyl)ethynyl]piperidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;

(4aR,8aS)-6-[3-[2-(2-Chlorophenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;

20 (4aR,8aS)-6-[3-[2-(2-Chloro-4-fluorophenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;

(4aR,8aS)-6-[4-[N-methyl-4-(trifluoromethyl)anilino]piperidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;

25 (4aR,8aS)-6-(3-(((2-Chloro-4-(trifluoromethyl)phenyl)thio)methyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;

(4aR,8aS)-6-(3-((2-Fluoro-4-(trifluoromethyl)benzyl)thio)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;

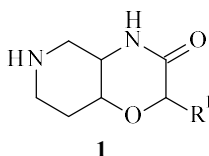
(4aR,8aS)-6-(3-((2,6-Dichlorophenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;

30 (4aR,8aS)-6-[3-[2-[2-Fluoro-4-(trifluoromethyl)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;

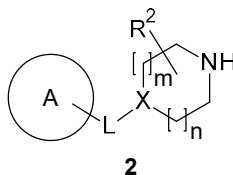
(4aR,8aS)-6-(3-((2-Chloro-6-fluorophenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;

- (4aR,8aS)-6-(3-((2-Chloro-4-cyclopropylphenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
 (4aR,8aS)-6-[3-[2-[4-Trifluoromethoxy)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
 5 (4aR,8aS)-6-[3-[2-(2,6-Dimethylphenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
 (4aR,8aS)-6-[3-[2-[2-(Trifluoromethoxy)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
 (4aR,8aS)-6-(3-(o-Tolylethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one;
 10 (4aR,8aS)-6-[3-[2-(4-Chloro-2-fluorophenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
 (4aR,8aS)-6-[3-[2-[2-(Difluoromethyl)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
 15 (4aR,8aS)-6-[3-[2-(2-Chloro-6-methylphenyl)ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one;
 (4aR,8aS)-6-[3-[2-[2-Chloro-6-fluoro-4-(trifluoromethyl)phenyl]ethynyl]azetidine-1-carbonyl]-4,4a,5,7,8,8a-hexahydropyrido[4,3-b][1,4]oxazin-3-one; and
 (4aR,8aS)-6-(3-((2-Chloro-4-(trifluoromethyl)phenyl)ethynyl)azetidine-1-carbonyl)hexahydro-2H-pyrido[4,3-b][1,4]oxazin-3(4H)-one.
 20

40:11. A process of manufacturing the compounds of formula (I) according to any one of claims 1 to 1039, comprising:
 reacting a first amine of formula **1**, wherein R¹ is as described in any one of claims 1 to 1039,



with a second amine **2**, wherein A, L, m, n, X and R² are as described in any one of claims 1 to 1039



in the presence of a base and a urea forming reagent,
to form said compound of formula (I).

~~41.—A compound of formula (I) according to any one of claims 1 to 39, when
manufactured according to the process of claim 40.~~

5 ~~42.—The compound of formula (I) according to any one of claims 1 to 39 and 41, wherein
said compound of formula (I) has an IC₅₀ for monoacylglycerol lipase below 10 µM,
preferably below 5 µM.~~

~~43.12. _____~~ A compound of formula (I) according to any one of claims 1 to ~~39, 41 and~~
~~4210~~ for use as therapeutically active substance.

10 ~~44.13. _____~~ A pharmaceutical composition comprising a compound of formula (I)
according to any one of claims 1 to ~~1039, 41 and 42~~ and a therapeutically inert
carrier.

15 ~~45.—The use of a compound of formula (I) according to any one of claims 1 to 39, 41 and
42 or of a pharmaceutical composition according to claim 44 for the treatment or
prophylaxis of neuroinflammation, neurodegenerative diseases, pain, cancer and/or
mental disorders in a mammal.~~

20 ~~46.—The use of a compound of formula (I) according to any one of claims 1 to 39, 41 and
42 or of a pharmaceutical composition according to claim 44 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 and/or spasticity associated with pain in a mammal.~~

25 ~~47.14. _____~~ A compound of formula (I) according to any one of claims 1 to ~~39, 41 and~~
~~4210~~ or ~~of~~ a pharmaceutical composition according to claim ~~44 13~~ for use in the
treatment or prophylaxis of neuroinflammation, neurodegenerative diseases, pain,
cancer and/or mental disorders in a mammal.

30 ~~48.15. _____~~ A compound of formula (I) according to any one of claims 1 to ~~39, 41 and~~
~~4210~~ or ~~of~~ a pharmaceutical composition according to claim ~~44 13~~ 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 and/or spasticity associated with pain in a mammal.

5 ~~49.16.~~ 16. The use of a compound of formula (I) according to any one of claims 1 to ~~39,~~
~~41 and 42~~ 10 or a pharmaceutical composition according to claim ~~13~~ 13 ~~for in~~ the
preparation of a medicament for the treatment or prophylaxis of neuroinflammation,
neurodegenerative diseases, pain, cancer and/or mental disorders in a mammal.

10 ~~50.17.~~ 17. The use of a compound of formula (I) according to any one of claims 1 to ~~39,~~
~~41 and 42~~ 10 or a pharmaceutical composition according to claim ~~13~~ 13 ~~for in~~ 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,
15 hepatocellular carcinoma, colon carcinogenesis, ovarian cancer, neuropathic pain,
chemotherapy induced neuropathy, acute pain, chronic pain and/or spasticity
associated with pain in a mammal.

20 ~~51.—A method for the treatment or prophylaxis of neuroinflammation, neurodegenerative
diseases, pain, cancer and/or mental disorders in a mammal, which method
comprises administering an effective amount of a compound of formula (I)
according to any one of claims 1 to 39, 41 and 42 or of a pharmaceutical
composition according to claim 44 to the mammal.~~

25 ~~52.—A method 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 and/or spasticity associated with pain
in a mammal, which method comprises administering an effective amount of a
compound of formula (I) according to any one of claims 1 to 39, 41 and 42 or of a
pharmaceutical composition according to claim 44 to the mammal.~~

53. ~~A method for determining the MAGL inhibitory activity of a test compound, e.g. of a compound according to any one of claims 1 to 39, 41 and 42, comprising measuring the ratio of arachidonic acid / d8-arachidonic acid in a solution.~~