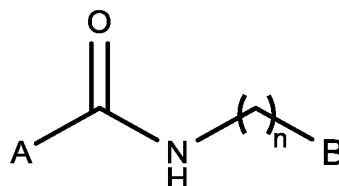


CLAIMS

1. A compound of formula (I) or (Ia),

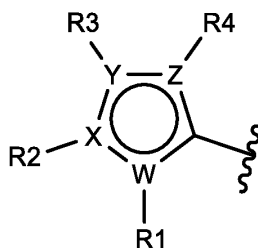


Formula (I)

wherein:

n is 0, 1, or 2;

A is (i) a 5- membered heteroaryl of formula (II),



Formula (II)

wherein W is S;

Z is C or N;

X and Y are C;

R1 is absent;

R4 is absent or H;

R2 and R3 are independently selected from H, halo, alkyl, -SO₂NR₁₃R₁₄,

-(CH₂)₀₋₃heterocyclyl, -(CH₂)₀₋₃NR₁₂(CH₂)₀₋₃(heterocyclyl), and -(CH₂)₀₋₃aryl; and

wherein one of R2 or R3 is not H; or

wherein W is S;

X, Y and Z are C;

R1 is absent;

R3 is halo or alkyl;

R4 is H, halo, or alkyl; and

R2 is selected from $-(CH_2)_{0-3}NR_{13}R_{14}$, $-(CH_2)_{0-3}NR_{12}(CH_2)_{0-3}(aryl)$,

$-(CH_2)_{0-3}NR_{12}(CH_2)_{0-3}(heterocyclyl)$, $-(CH_2)_{0-3}O-(CH_2)_{0-3}(aryl)$,

$-(CH_2)_{0-3}O-(CH_2)_{0-3}(heterocyclyl)$, $-(CH_2)_{0-3}O-(CH_2)_{0-3}(heteroaryl)$,

5 $-(CH_2)_{0-3}O-(CH_2)_{1-4}NR_{13}R_{14}$, and $-(CH_2)_{0-3}heterocyclyl$; or

wherein X, Y and Z are independently N, C or S;

wherein at least one of X, Y and Z is N or S;

W is C;

10 R3 and R4 are independently absent or independently selected from H, alkyl and halo;

R2 is selected from H, halo, alkyl, and cycloalkyl; and

R1 is selected from $-(CH_2)_{0-3}NR_{12}(CH_2)_{0-3}(heterocyclyl)$,

$-(CH_2)_{0-3}NR_{12}CO(CH_2)_{0-3}(heterocyclyl)$, $-(CH_2)_{0-3}O-(CH_2)_{0-3}(heterocyclyl)$, and

$-(CH_2)_{0-3}heterocyclyl$; or

15

wherein Y and Z are N;

W and X are C;

R1 and R2 are selected from H, halo, alkyl, cycloalkyl, and $-(CH_2)_{0-3}aryl$;

R3 and R4 are independently absent or independently selected from

20 $-(CH_2)_{0-3}heterocyclyl$, and $-(CH_2)_{0-3}aryl$; and

wherein at least one of R3 or R4 is selected from $-(CH_2)_{0-3}heterocyclyl$, and

$-(CH_2)_{0-3}aryl$; or

wherein Y or Z are independently C, N or S;

25 wherein at least one of Y and Z is N or S;

W and X are C;

R1 is H;

R2 is selected from H, alkyl, aryl, and halo;

R4 is absent, or selected from H and alkyl; and

30 R3 is $(CH_2)_{0-3}(heterocyclyl)$; or

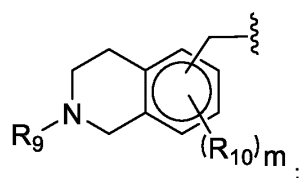
wherein Y and X are independently C or N;

wherein at least one of Y or X is N;

W and Z are C;

35 R1 and R4 are independently selected from H, alkyl, and halo; and

one of R2 and R3 is absent and the other of R2 and R3 is

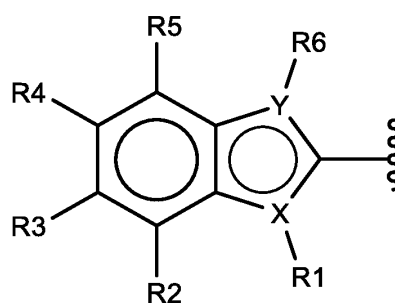


m is 0, 1, 2, or 3;

R9 is selected from H and alkyl;

Each R10 is independently selected from alkyl and halo; or

A is (ii) a 9- membered heteroaromatic bicycle of formula (III)



Formula (III)

wherein X and Y are independently selected from C, N or S;

wherein at least one of X and Y is N or S;

wherein R1 and R6 are independently absent or independently selected from H and $-(CH_2)_{0-3}$ heterocyclyl;

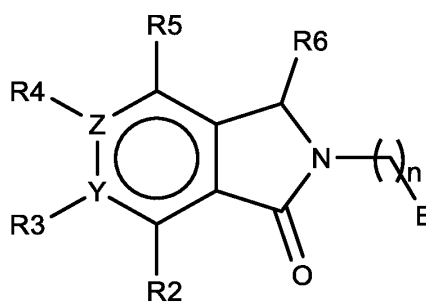
wherein R2 is selected from H, halo, $-(CH_2)_{0-3}NR_{12}(CH_2)_{0-3}$ (heterocyclyl), and $-(CH_2)_{0-3}$ heterocyclyl;

R3, R4, and R5 are independently selected from H, alkyl and halo; and

wherein at least one of R2, R3, R4, R5 is not absent or H;

or,

226



Formula (Ia)

wherein n is 0, 1, or 2;

wherein Z and Y are independently selected from C and N;

wherein R6 is selected from H and alkyl;

wherein R4 and R5 are independently absent, or independently selected from H, alkyl, and halo; and

wherein one of R2 and R5 is $-(CH_2)_{0-3}NR_{12}(CH_2)_{0-3}(\text{heterocycl})$, and the other of R2 and R5 is selected from H, alkyl, and halo;

B is:

(i) a fused 6,5- or 6,6- heteroaromatic bicyclic ring, containing N and, optionally, one or two additional heteroatoms independently selected from N, O and S;

wherein the fused 6,5- or 6,6- heteroaromatic bicyclic ring may be optionally substituted with 1, 2, or 3 substituents selected from alkyl, alkoxy, OH, halo, CN, $-COOR_{13}$, $-CONR_{13}R_{14}$, CF_3 and $-NR_{13}R_{14}$;

wherein the 6,5- heteroaromatic bicyclic ring may be attached *via* the 6- or 5-membered ring; or

(ii) phenyl substituted with $-(CH_2)_{1-3}NH_2$ and two groups selected from methyl, ethyl and propyl; or

(iii) pyridine substituted with NH_2 and two groups selected from methyl, ethyl and propyl;

(iv) a fused 6,5- or 6,6- bicyclic ring containing N and containing an aromatic ring fused to a non-aromatic ring and, optionally, one or two additional heteroatoms independently selected from N, O and S;

wherein the fused 6,5- or 6,6- bicyclic ring may be optionally substituted with 1, 2, or 3 substituents selected from alkyl, alkoxy, OH, halo, CN, -COOR₁₃, -CONR₁₃R₁₄, CF₃ and -NR₁₃R₁₄;

wherein the 6,5- bicyclic ring may be attached *via* the 6- or 5- membered ring;

5

alkoxy is a linear O-linked hydrocarbon of between 1 and 6 carbon atoms (C₁-C₆) or a branched O-linked hydrocarbon of between 3 and 6 carbon atoms (C₃-C₆); alkoxy may optionally be substituted with 1 or 2 substituents independently selected from OH, CN, CF₃, -N(R₁₂)₂ and fluoro;

10

alkyl is a linear saturated hydrocarbon having up to 10 carbon atoms (C₁-C₁₀) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C₃-C₁₀); alkyl may optionally be substituted with 1 or 2 substituents independently selected from (C₁-C₆)alkoxy, OH, -NR₁₃R₁₄, -NHCOCH₃, -CO(heterocycl^byl), -COOR₁₃, -CONR₁₃R₁₄, CN, CF₃, halo, oxo, and heterocycl^byl;

15

alkyl^b is a linear saturated hydrocarbon having up to 10 carbon atoms (C₁-C₁₀) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C₃-C₁₀); alkyl may optionally be substituted with 1 or 2 substituents independently selected from (C₁-C₆)alkoxy, OH, -N(R₁₂)₂, -NHCOCH₃, CF₃, halo, oxo, cyclopropane, -O(aryl^b), aryl^b, and heterocycl^byl;

20

alkylene is a bivalent linear saturated hydrocarbon having 1 to 5 carbon atoms (C₁-C₅); alkylene may optionally be substituted with 1 or 2 substituents independently selected from alkyl, (C₁-C₆)alkoxy, OH, CN, CF₃, and halo;

25

aryl is phenyl, biphenyl or naphthyl; aryl may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, -SO₂CH₃, halo, CN, -(CH₂)₀₋₃-O-heteroaryl^b, aryl^b, -O-aryl^b, -(CH₂)₀₋₃-heterocycl^byl, -(CH₂)₁₋₃-aryl^b, -(CH₂)₀₋₃-heteroaryl^b, -COOR₁₃, -CONR₁₃R₁₄, -(CH₂)₀₋₃-NR₁₃R₁₄, OCF₃ and CF₃; or two adjacent carbon ring atoms on the aryl may be optionally linked by a heteroalkylene to form a non-aromatic ring containing 5, 6, or 7 ring members; or optionally wherein two adjacent ring atoms on aryl are linked to form a 5- or 6- membered aromatic ring containing 1 or 2 heteroatoms that are selected from N, NR₈, S, and O;

30

aryl^b is phenyl, biphenyl or naphthyl, which may be optionally substituted with 1, 2 or 3 substituents independently selected from methyl, ethyl, propyl, isopropyl, alkoxy, OH, -SO₂CH₃, N(R₁₂)₂, halo, CN,

and CF₃; or two adjacent carbon ring atoms on the aryl may be optionally linked by a heteroalkylene to form a non-aromatic ring containing 5, 6, or 7 ring members;

cycloalkyl is a monocyclic saturated hydrocarbon ring of between 3 and 6 carbon atoms (C₃-C₆);

- 5 cycloalkyl may optionally be substituted with 1 or 2 substituents independently selected from alkyl^b, (C₁-C₆)alkoxy, OH, CN, CF₃, and halo;

halo is F, Cl, Br, or I;

- 10 heteroalkylene is a bivalent linear saturated hydrocarbon having 2 to 5 carbon atoms (C₂-C₅), wherein 1 or 2 of the 2 to 5 carbon atoms are replaced with NR₈, S, or O; heteroalkylene may optionally be substituted with 1 or 2 substituents independently selected from alkyl (C₁-C₆)alkoxy, OH, CN, CF₃, and halo;

- 15 heteroaryl is a 5- or 6- membered carbon-containing aromatic ring containing 1, 2, 3, or 4 ring members that are selected from N, NR₈, S, and O; heteroaryl may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, aryl^b, OH, OCF₃, halo, heterocyclyl^b, CN, and CF₃;

- heteroaryl^b is a 5- or 6- membered carbon-containing aromatic ring containing one, two or three ring
20 members that are selected from N, NR₈, S, and O; heteroaryl^b may be optionally substituted with 1, 2 or 3 substituents independently selected from methyl, ethyl, propyl, isopropyl, alkoxy, OH, OCF₃, halo, CN, and CF₃;

- heterocyclyl is a 4-, 5-, 6-, or 7- membered carbon-containing non-aromatic ring containing one or two
25 ring members that are selected from N, NR₈, S, SO, SO₂ and O; heterocyclyl may be optionally substituted with 1, 2, 3, or 4 substituents independently selected from alkyl^b, alkoxy, OH, OCF₃, halo, oxo, CN, -NR₁₃R₁₄, -O(aryl^b), -O(heteroaryl^b) and CF₃; or optionally wherein two ring atoms on heterocyclyl are linked with an alkylene to form a non-aromatic ring containing 5, 6, or 7 ring members; or optionally wherein two adjacent ring atoms on heterocyclyl are linked to form a 5- or 6- membered
30 aromatic ring containing 1 or 2 heteroatoms that are selected from N, NR₈, S, and O; or optionally wherein a carbon ring atom on heterocyclyl is substituted with a heteroalkylene such that the carbon ring atom on heterocyclyl together with the heteroalkylene forms a heterocyclyl^b that is spiro to ring heterocyclyl;

heterocyclyl^b is a 4-, 5-, 6-, or 7- membered carbon-containing non-aromatic ring containing one or two ring members that are selected from N, NR₁₂, S, SO, SO₂ and O; heterocyclyl^b may be optionally substituted with 1, 2, 3, or 4 substituents independently selected from methyl, ethyl, propyl, isopropyl, alkoxy, OH, OCF₃, halo, oxo, CN, and CF₃;

5

R₁₃ and R₁₄ are independently selected from H, -SO₂CH₃, alkyl^b, heteroaryl^b, and cycloalkyl; or R₁₃ and R₁₄ together with the nitrogen atom to which they are attached form a carbon-containing 4-, 5-, 6- or 7-membered heterocyclic ring, optionally containing an additional heteroatom selected from N, NR₈, S, SO, SO₂, and O, which may be saturated or unsaturated with 1 or 2 double bonds and which may be optionally mono- or di-substituted with substituents independently selected from oxo, alkyl^b, alkoxy, OH, halo, -SO₂CH₃, and CF₃; or R₁₃ and R₁₄ together with the nitrogen atom to which they are attached form a carbon-containing 5- or 6- membered heterocyclic ring, which is fused to an aryl^b or a heteroaryl^b;

10

R₈ is independently selected from H, -SO₂CH₃, alkyl^b, -(CH₂)₀₋₃aryl^b, -(CH₂)₀₋₃heteroaryl^b, -(CH₂)₀₋₃cycloalkyl, and -(CH₂)₀₋₃heterocyclyl^b; or R₈ is a carbon-containing 4-, 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 heteroatoms independently selected from N, N₁₂, S, SO, SO₂, and O, which may be saturated or unsaturated with 1 or 2 double bonds and which may be optionally mono- or di-substituted with substituents independently selected from oxo, alkyl^b, alkoxy, OH, halo, -SO₂CH₃, and CF₃;

15

20

R₁₂ is independently selected from H, -SO₂CH₃, -COCH₃, methyl, ethyl, propyl, isopropyl, and cycloalkyl;

and tautomers, isomers, stereoisomers (including enantiomers, diastereoisomers and racemic and scalemic mixtures thereof), deuterated isotopes, and pharmaceutically acceptable salts and/or solvates thereof.

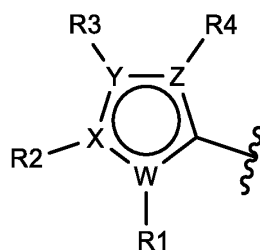
25

2. A compound of formula (I) according to claim 1, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

30

wherein A is a 5- membered heteroaryl of formula (II),

230



Formula (II)

wherein W is S;

Z is C or N;

X and Y are C;

R1 is absent;

R4 is absent or H;

R2 and R3 are independently selected from H, halo, alkyl, $-\text{SO}_2\text{NR}_{13}\text{R}_{14}$,

$-(\text{CH}_2)_{0-3}\text{heterocyclyl}$, $-(\text{CH}_2)_{0-3}\text{NR}_{12}(\text{CH}_2)_{0-3}(\text{heterocyclyl})$, and $-(\text{CH}_2)_{0-3}\text{aryl}$; and

wherein one of R2 or R3 is not H.

3. A compound of formula (I) according to claim 2, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

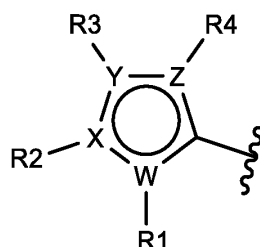
wherein at least one of R2 and R3 is either (i) halo, or (ii) selected from $-(\text{CH}_2)_{0-3}\text{heterocyclyl}$, $-(\text{CH}_2)_{0-3}\text{NR}_{12}(\text{CH}_2)_{0-3}(\text{heterocyclyl})$, and $-(\text{CH}_2)_{0-3}\text{aryl}$.

4. A compound of formula (I) according to any of claims 1 to 3, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein R2 is alkyl and R3 is halo.

5. A compound of formula (I) according to any of claims 1 to 3, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein R2 is H and R3 is $-(\text{CH}_2)_{0-3}\text{heterocyclyl}$.

6. A compound of formula (I) according to claim 1, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is a 5- membered heteroaryl of formula (II),



Formula (II)

wherein W is S;

X, Y and Z are C;

R1 is absent;

R3 is halo or alkyl;

R4 is H, halo, or alkyl; and

R2 is selected from $-(CH_2)_{0-3}NR_{13}R_{14}$, $-(CH_2)_{0-3}NR_{12}(CH_2)_{0-3}(aryl)$,

$-(CH_2)_{0-3}NR_{12}(CH_2)_{0-3}(heterocyclyl)$, $-(CH_2)_{0-3}O-(CH_2)_{0-3}(aryl)$,

$-(CH_2)_{0-3}O-(CH_2)_{0-3}(heterocyclyl)$, $-(CH_2)_{0-3}O-(CH_2)_{0-3}(heteroaryl)$,

$-(CH_2)_{0-3}O-(CH_2)_{1-4}NR_{13}R_{14}$, and $-(CH_2)_{0-3}heterocyclyl$.

7. A compound of formula (I) according to claim 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein R3 is halo.

8. A compound of formula (I) according to claim 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

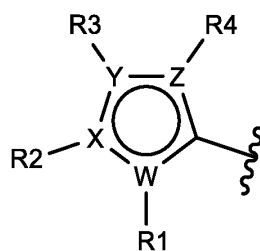
wherein R3 is alkyl.

9. A compound of formula (I) according to any of claims 6 to 7, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein R4 is H and R2 is $-(CH_2)_{0-3}NR_{13}R_{14}$.

10. A compound of formula (I) according to claim 1, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

5 wherein A is a 5- membered heteroaryl of formula (II),



Formula (II)

wherein X, Y and Z are independently N, C or S;

10 wherein at least one of X, Y and Z is N or S;

W is C;

R3 and R4 are independently absent or independently selected from H, alkyl and halo;

R2 is selected from H, halo, alkyl, and cycloalkyl; and

R1 is selected from $-(CH_2)_{0-3}NR_{12}(CH_2)_{0-3}(\text{heterocyclyl})$,

15 $-(CH_2)_{0-3}NR_{12}CO(CH_2)_{0-3}(\text{heterocyclyl})$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}(\text{heterocyclyl})$, and $-(CH_2)_{0-3}\text{heterocyclyl}$.

11. A compound of formula (I) according to claim 10, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

20 wherein Z is S, and Y and X and C.

12. A compound of formula (I) according to claim 10, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

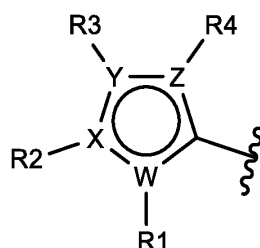
25 wherein Z is S, Y is C, and X is N.

13. A compound of formula (I) according to any of claims 10 to 13, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

30

wherein R1 is $-(CH_2)_{0-3}NR^{12}(CH_2)_{0-3}(\text{heterocycl})$.

14. A compound of formula (I) according to claim 1, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
- 5 wherein A is a 5- membered heteroaryl of formula (II),



Formula (II)

- wherein Y and Z are N ;
- 10 W and X are C;
- R1 and R2 are selected from H, halo, alkyl, cycloalkyl, and $-(CH_2)_{0-3}\text{aryl}$;
- R3 and R4 are independently absent or independently selected from $-(CH_2)_{0-3}\text{heterocycl}$, and $-(CH_2)_{0-3}\text{aryl}$; and
- wherein at least one of R3 or R4 is selected from $-(CH_2)_{0-3}\text{heterocycl}$, and
- 15 $-(CH_2)_{0-3}\text{aryl}$.

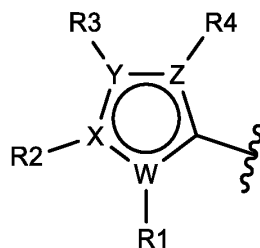
15. A compound of formula (I) according to claim 14, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
- 20 wherein R2 is halo.

16. A compound of formula (I) according to claim 14, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
- wherein R2 is H.

- 25 17. A compound of formula (I) according to any of claims 14 to 16, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
- wherein R4 is $-(CH_2)_{0-3}\text{heterocycl}$.

18. A compound of formula (I) according to claim 1, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is a 5- membered heteroaryl of formula (II),



Formula (II)

wherein Y or Z are independently C, N or S;

wherein at least one of Y and Z is N or S;

W and X are C;

R1 is H;

R2 is selected from H, alkyl, aryl, and halo;

R4 is absent, or selected from H and alkyl; and

R3 is $-(CH_2)_{0-3}(\text{heterocycl})$.

19. A compound of formula (I) according to claim 18, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein Z is N.

20. A compound of formula (I) according to any of claims 18 to 19, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

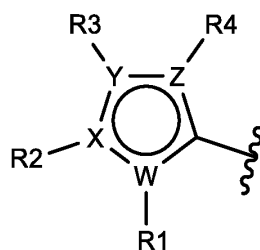
wherein Y is N.

21. A compound of formula (I) according to any of claims 18 to 20, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein R3 is $-(CH_2)_{0-3}(\text{heterocycl})$.

22. A compound of formula (I) according to claim 1, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is a 5- membered heteroaryl of formula (II),



Formula (II)

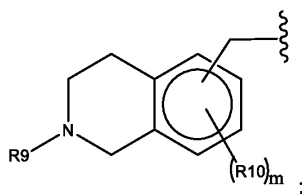
wherein Y and X are independently C or N;

wherein at least one of Y or X is N;

W and Z are C;

R1 and R4 are independently selected from H, alkyl, and halo; and

one of R2 and R3 is absent and the other of R2 and R3 is

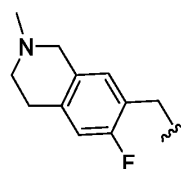


m is 0, 1, 2, or 3;

R9 is selected from H and alkyl;

Each R10 is independently selected from alkyl and halo.

23. A compound of formula (I) according to claim 22, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

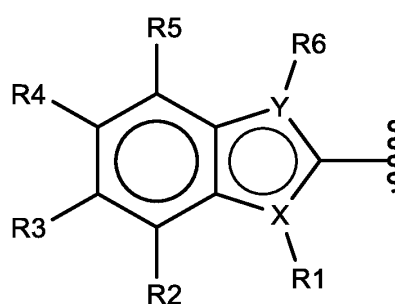


wherein one of R2 and R3 is absent and the other of R2 and R3 is

24. A compound of formula (I) according to any of claims 22 to 23, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein R1 is alkyl, preferably -CH₂OCH₃.

5

25. A compound of formula (I) according to claim 1, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein A is a 9- membered heteroaromatic bicycle of formula (III)



10

Formula (III)

wherein X and Y are independently selected from C, N or S;

wherein at least one of X and Y is N or S;

15

wherein R1 and R6 are independently absent or independently selected from H and -(CH₂)₀₋₃heterocyclyl;

wherein R2 is selected from H, halo, -(CH₂)₀₋₃NR₁₂(CH₂)₀₋₃(heterocyclyl), and -(CH₂)₀₋₃heterocyclyl;

R3, R4, and R5 are independently selected from H, alkyl and halo; and

20

wherein at least one of R1, R2, R3, R4, R5 and R6 is not H.

26. A compound of formula (I) according to claim 25, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

25

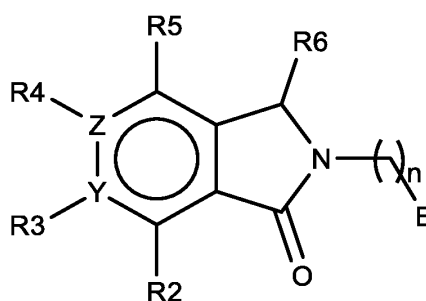
wherein Y is S.

27. A compound of formula (I) according to claim 25, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein Y is N.

28. A compound of formula (I) according to any of claims 25 to 27, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein R2 is chloro.

29. A compound of formula (I) according to claim 1, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein A is a compound of formula (Ia),



Formula (Ia)

- wherein n is 0, 1, or 2;
 wherein Z and Y are independently selected from C and N;
 wherein R6 is selected from H and alkyl;
 wherein R4 and R5 are independently absent, or independently selected from H, alkyl, and halo; and
 wherein one of R2 and R5 is $-(CH_2)_{0-3}NR^{12}(CH_2)_{0-3}(\text{heterocyclyl})$, and the other of R2 and R5 is selected from H, alkyl, and halo.

30. A compound of formula (I) according to claim 29, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein R2 can be $-(CH_2)_{0-3}NR^{12}(CH_2)_{0-3}(\text{heterocyclyl})$.

31. A compound selected from any of Tables 1 to 12, and pharmaceutically acceptable salts and/or solvates thereof.

and pharmaceutically acceptable salts and/or solvates thereof.

5 32. A pharmaceutical composition comprising: a compound or a pharmaceutically acceptable salt and/or solvate thereof according to any preceding claim, and at least one pharmaceutically acceptable excipient.

10 33. A compound, or a pharmaceutically acceptable salt and/or solvate thereof, as claimed in any of claims 1 to 31, or the pharmaceutical composition as claimed in claim 32, for use in medicine.

15 34. The use of a compound or a pharmaceutically acceptable salt and/or solvate thereof according to any of claims 1 to 31, or the pharmaceutical composition as claimed in claim 32, in the manufacture of a medicament for the treatment or prevention of a disease or condition in which Factor XIIa activity is implicated.

20 35. A method of treatment of a disease or condition in which Factor XIIa activity is implicated comprising administration to a subject in need thereof a therapeutically effective amount of a compound or a pharmaceutically acceptable salt and/or solvate thereof according to any of claims 1 to 31, or the pharmaceutical composition as claimed in claim 32.

25 36. A compound or a pharmaceutically acceptable salt and/or solvate thereof according to any of claims 1 to 31, or a pharmaceutical composition as claimed in claim 32, for use in a method of treatment of a disease or condition in which Factor XIIa activity is implicated.

30 37. The use of claim 34, the method of claim 35, or a compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as claimed in claim 36, wherein, the disease or condition in which Factor XIIa activity is implicated is a bradykinin-mediated angioedema.

35 38. The use of claim 37, the method of claim 37, or a compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as claimed in claim 37, wherein the bradykinin-mediated angioedema is hereditary angioedema.

39. The use of claim 37, the method of claim 37, or a compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as claimed in claim 37, wherein the bradykinin-mediated angioedema is non hereditary.

40. The use of claim 34, the method of claim 35, or a compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as claimed in claim 36, wherein the disease or condition in which Factor XIIa activity is implicated is selected from vascular hyperpermeability; stroke including ischemic stroke and haemorrhagic accidents; retinal edema; diabetic retinopathy; DME; retinal vein occlusion; and AMD.
41. The use of claim 34, the method of claim 35, or a compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as claimed in claim 36, wherein, the disease or condition in which Factor XIIa activity is implicated is a thrombotic disorder.
42. The use of claim 41, the method of claim 41, or a compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as defined in claim 41, wherein the thrombotic disorder is thrombosis; thromboembolism caused by increased propensity of medical devices that come into contact with blood to clot blood; prothrombotic conditions such as disseminated intravascular coagulation (DIC), Venous thromboembolism (VTE), cancer associated thrombosis, complications caused by mechanical and bioprosthetic heart valves, complications caused by catheters, complications caused by ECMO, complications caused by LVAD, complications caused by dialysis, complications caused by CPB, sickle cell disease, joint arthroplasty, thrombosis induced to tPA, Paget Schroetter syndrome and Budd-Chari syndrome; and atherosclerosis.
43. The use of claim 34, the method of claim 35, or a compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as claimed in claim 36, wherein, the disease or condition in which Factor XIIa activity is implicated is selected from neuroinflammation; neuroinflammatory/neurodegenerative disorders such as MS (multiple sclerosis); other neurodegenerative diseases such as Alzheimer's disease, epilepsy and migraine; sepsis; bacterial sepsis; inflammation; vascular hyperpermeability; and anaphylaxis.
44. The use of any of claims 34 or 37 to 43, the method of any of claims 35 or 37 to 43, or a compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as defined in any of claims 36 or 37 to 43, wherein the compound targets FXIIa.