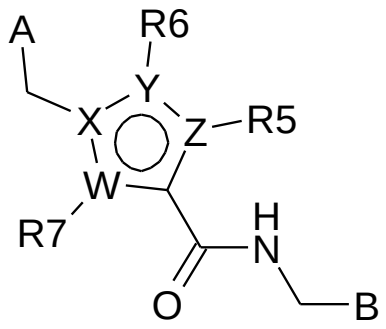
Claims

1. A compound of formula (I),



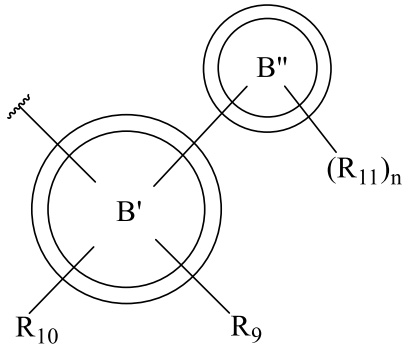
Formula (I)

wherein

W, X, Y and Z are independently selected from C, C(R16)-C, C(R16)=C, C=N, O and N, such that the ring containing W, X, Y and Z is a 5-, or 6- membered heteroaryl;
R5, R6, and R7 are independently absent or independently selected from H, alkyl, cycloalkyl, alkoxy, halo, OH, CN, CF_3, aryl, heteroaryl[a], N-linked pyrrolidinyl, N-linked piperidinyl, N-linked morpholinyl, N-linked piperazinyl, -NR13R14, -COOR13, -CONR13R14, and -NR13COR14;
R16 is independently selected from H, alkyl, cycloalkyl, alkoxy, halo, OH, CN, CF_3, aryl, heteroaryl[a], N-linked pyrrolidinyl, N-linked piperidinyl, N-linked morpholinyl, N-linked piperazinyl, -NR13R14, -COOR13, -CONR13R14, and -NR13COR14; or

W, X, Y and Z are independently selected from C, C(R16)-C, C(R16)=C, C=N and N, and one of R5, R6, R7 or R16 is oxo such that the ring containing W, X, Y and Z is 2-pyridone or 4-pyridone;
wherein the others of R5, R6, R7 and R16 are independently absent or independently selected from H, alkyl, cycloalkyl, alkoxy, halo, OH, CN, CF_3, aryl, heteroaryl[a], N-linked pyrrolidinyl, N-linked piperidinyl, N-linked morpholinyl, N-linked piperazinyl, -NR13R14, -COOR13,
-CONR13R14, and -NR13COR14;

B is of Formula (II) comprising aromatic rings B’ and B’’ that are linked by a bond:



Formula (II)

B’ is phenyl or pyridyl;

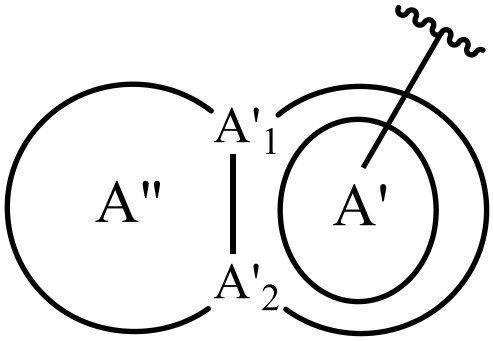
B’’ is pyrrole, pyrazole, triazole, or tetrazole;

n is 0, 1, or 2;

R9 and R10 are independently selected from H, alkyl, cycloalkyl, alkoxy, halo, OH, CN, and CF_3;

Each R11 is independently selected from alkyl, cycloalkyl, alkoxy, halo, OH, -COOR13, -CONR13NR14, CN, and CF_3;

A is a heterocyclic ring of Formula (III) comprising an aromatic ring (A’) fused to a non-aromatic ring (A’’):



Formula (III)

A’1 and A’2 are independently C or N;

A’ is heteroaryl or phenyl, wherein phenyl may be optionally substituted with 1, 2, or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, and CF_3, and wherein heteroaryl may be optionally substituted as stated below;

A’’ is heterocycloalkyl;

optionally wherein a carbon ring atom on A’’ is substituted with an alkylene or a heteroalkylene such that the carbon ring atom on A’’ together with the

alkylene or the heteroalkylene forms a cycloalkyl or heterocycloalkyl[a] that is spiro to ring A''; and/or
optionally wherein two ring atoms on A'' are linked by an alkylene or heteroalkylene to form a non-aromatic ring containing 5, 6, or 7 ring members;

alkyl is a linear saturated hydrocarbon having up to 10 carbon atoms (C_1-C_{10}) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C_3-C_{10}); alkyl may optionally be substituted with 1 or 2 substituents independently selected from (C_1-C_6)alkoxy, OH, -NR13R14, -COOR13, -CONR13R14, CN, CF_3, halo;

alkyl[b] is a linear saturated hydrocarbon having up to 10 carbon atoms (C_1-C_{10}) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C_3-C_{10}); alkyl[b] may optionally be substituted with 1 or 2 substituents independently selected from (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

alkylene is a bivalent linear saturated hydrocarbon having 1 to 5 carbon atoms (C_1-C_5); alkylene may optionally be substituted with 1 or 2 substituents independently selected from alkyl, (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

aryl is phenyl, biphenyl or naphthyl; aryl may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, methylenedioxy, ethylenedioxy, OH, halo, CN, heteroaryl[a], -$(CH_2)_{0-3}$-O-heteroaryl[a], aryl[b], -O-aryl[b], -$(CH_2)_{1-3}$-aryl[b], -$(CH_2)_{1-3}$-heteroaryl[a], -COOR13, -CONR13R14, -$(CH_2)_{0-3}$-NR13R14, OCF_3 and CF_3;

aryl[b] is phenyl, biphenyl or naphthyl; aryl[b] may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl[b], alkoxy, OH, halo, CN, and CF_3;

heteroalkylene is a bivalent linear saturated hydrocarbon having 2 to 5 carbon atoms (C_2-C_5), wherein at least one of the 2 to 5 carbon atoms is replaced with NR8, S, or O; heteroalkylene may optionally be substituted with 1 or 2 substituents independently selected from alkyl (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

cycloalkyl is a monocyclic saturated hydrocarbon ring of between 3 and 6 carbon atoms (C_3-C_6); cycloalkyl may optionally be substituted with 1 or 2 substituents independently selected from alkyl, (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

alkoxy is a linear O-linked hydrocarbon of between 1 and 6 carbon atoms (C_1-C_6) or a branched O-linked hydrocarbon of between 3 and 6 carbon atoms (C_3-C_6); alkoxy may optionally be substituted with 1 or 2 substituents independently selected from OH, CN, CF_3, and fluoro;

halo is F, Cl, Br, or I;

heteroaryl is a 5- or 6- membered carbon-containing aromatic ring containing one, two or three 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, OH, OCF_3, halo, CN, and CF_3;

heteroaryl[a] is a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O; heteroaryl[a] may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, aryl[b], -$(CH_2)_{1-3}$-aryl[b], -$(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -COOR13, -CONR13R14 and CF_3;

heteroaryl[b] is a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2 or 3 ring members independently selected from N, NR12, S and O; wherein heteroaryl[b] may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl[b], alkoxy, OH, halo, CN, aryl[b], -$(CH_2)_{1-3}$-aryl[b], and CF_3;

heterocycloalkyl is a non-aromatic carbon-containing monocyclic ring containing 5, 6, or 7 ring members, wherein one or two ring members are independently selected from N, NR8, S, SO, SO_2, and O; wherein heterocycloalkyl may be optionally substituted with 1, 2, or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, oxo and CN;

heterocycloalkyl[a] is a non-aromatic carbon-containing monocyclic ring containing 3, 4, 5, or 6, ring members, wherein at least one ring member is independently selected from NR8, S,

SO, SO_2, and O; heterocycloalkyl[a] may be optionally substituted with 1 or 2 substituents independently selected from alkyl (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

R8 is independently selected from H, alkyl, cycloalkyl, or heterocycloalkyl[b];

heterocycloalkyl[b] is a non-aromatic carbon-containing monocyclic ring containing 3, 4, 5, or 6, ring members, wherein at least one ring member is independently selected from N, NR12, S, and O; heterocycloalkyl[b] may be optionally be substituted with 1 or 2 substituents independently selected from alkyl, (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

R12 is independently selected from H, alkyl[b], or cycloalkyl;

R13 and R14 are independently selected from H, alkyl[b], aryl[b] and heteroaryl[b] or R13 and R14 together with the nitrogen atom to which they are attached form a carbon-containing 4-, 5-, 6- or 7-membered heterocylic ring, optionally containing an additional heteroatom selected from N, NR12, S, SO, SO_2, 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 selected from oxo, alkyl[b], alkoxy, OH, halo and CF_3;

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

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,

(a) wherein W, X, Y and Z are independently selected from C, C(R16)-C, C(R16)=C, C=N and N, such that the ring containing W, X, Y and Z is a 5-, or 6- membered heteroaryl;
R5, R6, and R7 are independently absent or independently selected from H, alkyl, cycloalkyl, alkoxy, halo, OH, CN, CF_3, aryl, heteroaryl[a], N-linked pyrrolidinyl, N-linked piperidinyl, N-linked morpholinyl, N-linked piperazinyl, -NR13R14, -COOR13, -CONR13R14, and -NR13COR14;

R16 is independently selected from H, alkyl, cycloalkyl, alkoxy, halo, OH, CN, CF_3, aryl, heteroaryl[a], N-linked pyrrolidinyl, N-linked piperidinyl, N-linked morpholinyl, N-linked piperazinyl, -NR13R14, -COOR13, -CONR13R14, and -NR13COR14; or

W, X, Y and Z are independently selected from C, C(R16)-C, C(R16)=C, C=N and N, and one of R5, R6, R7 or R16 is oxo such that the ring containing W, X, Y and Z is 2-pyridone or 4-pyridone;

wherein the others of R5, R6, R7 and R16 are independently absent or independently selected from H, alkyl, cycloalkyl, alkoxy, halo, OH, CN, CF_3, aryl, heteroaryl[a], N-linked pyrrolidinyl, N-linked piperidinyl, N-linked morpholinyl, N-linked piperazinyl, -NR13R14, -COOR13,

-CONR13R14, and -NR13COR14, and/or

(b) wherein W, X, Y and Z can independently be selected from C, C(R16)-C, C(R16)=C, C=N and N, such that the ring containing W, X, Y and Z is a 5-, or 6- membered heteroaryl;

R5, R6, and R7 are independently absent or independently selected from H, alkyl, cycloalkyl, alkoxy, halo, OH, CN, and CF_3;

R16 is independently selected from H, alkyl, cycloalkyl, alkoxy, halo, OH, CN, and CF_3; or

W, X, Y and Z are independently selected from C, C(R16)-C, C(R16)=C, C=N and N, and one of R5, R6, R7 or R16 is oxo such that the ring containing W, X, Y and Z is 2-pyridone or 4-pyridone;

wherein the others of R5, R6, R7 and R16 are independently absent or independently selected from H, alkyl, cycloalkyl, alkoxy, halo, OH, CN, and CF_3, and/or

(c) wherein W, X, Y and Z are independently selected from C, C(R16)-C, C(R16)=C, C=N and N, such that the ring containing W, X, Y and Z is a 5-, or 6- membered heteroaryl, and/or

(d) wherein W, X, Y and Z are independently selected from C and N, such that the ring containing W, X, Y and Z is a 5-membered heteroaryl, and/or

(e) wherein W, X, Y and Z are independently selected from C and N, such that the ring containing W, X, Y and Z is pyrazole, and/or

(f) wherein at least one of R5, R6, or R7 is present and is not H, and/or (g) wherein R7 is H, and/or (h) wherein one of R5 or R6 is absent and one of R5 or R6 is alkyl substituted with alkoxy, which may be optionally substituted as defined in claim 1, optionally wherein one of R5 or R6 is absent and one of R5 or R6 is -CH_2OMe, and/or

(i) wherein B' is phenyl, which may be substituted as defined in claim 1, and/or

(j) wherein R9 is halo and R10 is alkoxy, optionally,

wherein R9 is F and R10 is -OMe.

3. A compound of formula (I) according to claims 1 or 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 B'' pyrrole, pyrazole, or triazole, optionally, wherein B'' is pyrazole, or triazole, optionally,

(i) wherein B'' is pyrazole, which may be substituted as defined in claim 1, or

(ii) wherein B'' is 1, 2, 3-triazole, which may be substituted as defined in claim 1, or

(iii) wherein B'' is 1, 2, 4-triazole, which may be substituted as defined in claim 1.

4. A compound of formula (I) according to any of claims 1-3, 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 n is 1, and R11 is selected from alkyl, cyclopropyl, CN, and CF_3, and/or

wherein A' is phenyl, which may be optionally substituted as defined in claim 1, or

wherein A' is heteroaryl, which may be optionally substituted as defined in claim 1, optionally,

(i) wherein A' is a 5-membered heteroaryl, which may be optionally substituted as defined in claim 1, optionally

wherein A' is selected from pyrrole or imidazole, which may be optionally substituted as defined in claim 1, or

(ii) wherein A' is a 6-membered heteroaryl, which may be optionally substituted as defined in claim 1, for example, wherein A' is pyridine, which may be optionally substituted as defined in claim 1.

5. A compound of formula (I) according to any of claims 1-4, 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,

(i) wherein A'' is a non-aromatic carbon-containing monocyclic ring containing 5 ring members, wherein one or two ring members are independently selected from N, NR8, S, and O, which may be optionally substituted as defined in claim 1, optionally,

wherein A'' is pyrrolidine, which may be optionally substituted as defined in claim 1, or

(ii) wherein A'' is a non-aromatic carbon-containing monocyclic ring containing 6 ring members, wherein one or two ring members are independently selected from N, NR8, S, and O, which may be optionally substituted as defined in claim 1, optionally,

wherein A'' is piperidine, which may be optionally substituted as defined in claim 1, or

(iii) wherein A'' is a non-aromatic carbon-containing monocyclic ring containing 7 ring members, wherein one or two ring members are independently selected from N, NR8, S, and O, which may be optionally substituted as defined in claim 1, optionally,

wherein A'' is azepane, which may be optionally substituted as defined in claim 1.

6. A compound of formula (I) according to any of claims 1-5, 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 carbon ring atom on A'' is substituted with an alkylene such that the carbon ring atom on A'' together with the alkylene forms a cycloalkyl that is spiro to ring A'', which may be optionally substituted as defined in claim 1, and/or

wherein a carbon ring atom on A'' is substituted with an alkylene such that the carbon ring atom on A'' together with the alkylene forms a cyclopropane that is spiro to ring A'', which may be optionally substituted as defined in claim 1.

7. A compound of formula (I) according to any of claims 1 -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 two ring atoms on A'' are linked by an alkylene or heteroalkylene to form a non-aromatic ring containing 5, 6, or 7 ring members.

8. A compound selected from:

N-({6-[4-(difluoromethyl)-1,2,3-triazol-1-yl]-2-fluoro-3-methoxyphenyl}methyl)-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]pyrazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]pyrazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(3-methyl-1,2,4-triazol-1-yl)phenyl]methyl}-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]pyrazole-4-carboxamide;

N-{[6-(3-cyanopyrazol-1-yl)-2-fluoro-3-methoxyphenyl]methyl}-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]pyrazole-4-carboxamide;

N-({2-fluoro-3-methoxy-6-[3-(trifluoromethyl)-1,2,4-triazol-1-yl]phenyl}methyl)-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]pyrazole-4-carboxamide;

N-({6-[3-(difluoromethyl)-1,2,4-triazol-1-yl]-2-fluoro-3-methoxyphenyl}methyl)-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]pyrazole-4-carboxamide;

N-({2-fluoro-3-methoxy-6-[3-(trifluoromethyl)-1,2,4-triazol-1-yl]phenyl}methyl)-1-[(2-isopropyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

N-({6-[3-(difluoromethyl)-1,2,4-triazol-1-yl]-2-fluoro-3-methoxyphenyl}methyl)-1-[(2-isopropyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

N-{[6-(3-cyanopyrazol-1-yl)-2-fluoro-3-methoxyphenyl]methyl}-1-[(2-isopropyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

1-[(2-ethyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]-N-({2-fluoro-3-methoxy-6-[3-(trifluoromethyl)-1,2,4-triazol-1-yl]phenyl}methyl)-3-(methoxymethyl)pyrazole-4-carboxamide;

N-({6-[3-(difluoromethyl)-1,2,4-triazol-1-yl]-2-fluoro-3-methoxyphenyl}methyl)-1-[(2-ethyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

N-{[6-(3-cyanopyrazol-1-yl)-2-fluoro-3-methoxyphenyl]methyl}-1-[(2-ethyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

N-{[6-(4-cyanopyrazol-1-yl)-2-fluoro-3-methoxyphenyl]methyl}-1-[(2-isopropyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

N-({6-[4-(difluoromethyl)-1,2,3-triazol-1-yl]-2-fluoro-3-methoxyphenyl}methyl)-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]pyrazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]pyrazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-1-[(2-isopropyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

1-[(2-ethyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]-N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-3-(methoxymethyl)pyrazole-4-carboxamide;

N-({6-[3-(difluoromethyl)-1,2,4-triazol-1-yl]-2-fluoro-3-methoxyphenyl}methyl)-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]pyrazole-4-carboxamide;

N-({2-fluoro-3-methoxy-6-[3-(trifluoromethyl)-1,2,4-triazol-1-yl]phenyl}methyl)-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]pyrazole-4-carboxamide;

N-{[6-(3-cyanopyrazol-1-yl)-2-fluoro-3-methoxyphenyl]methyl}-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]pyrazole-4-carboxamide;

N-({6-[3-(difluoromethyl)-1,2,4-triazol-1-yl]-2-fluoro-3-methoxyphenyl}methyl)-1-[(2-isopropyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

N-({2-fluoro-3-methoxy-6-[3-(trifluoromethyl)-1,2,4-triazol-1-yl]phenyl}methyl)-1-[(2-isopropyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

N-{[6-(3-cyanopyrazol-1-yl)-2-fluoro-3-methoxyphenyl]methyl}-1-[(2-isopropyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

N-({6-[3-(difluoromethyl)-1,2,4-triazol-1-yl]-2-fluoro-3-methoxyphenyl}methyl)-1-[(2-ethyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

1-[(2-ethyl-3,4-dihydro-1H-isoquinolin-6-yl)methyl]-N-({2-fluoro-3-methoxy-6-[3-(trifluoromethyl)-1,2,4-triazol-1-yl]phenyl}methyl)-3-(methoxymethyl)pyrazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-3-(methoxymethyl)-1-[(2-methyl-1,3-dihydroisoindol-5-yl)methyl]pyrazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-1-[(2-isopropyl-1,3-dihydroisoindol-5-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

1-[(6-fluoro-2-methyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]-N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-3-(methoxymethyl)pyrazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-3-(methoxymethyl)-1-{[2-($^{2}H_{3}$)methyl-3,4-dihydro-1H-isoquinolin-7-yl]methyl}pyrazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-1-[(3-isopropyl-1,2,4,5-tetrahydro-3-benzazepin-7-yl)methyl]-3-(methoxymethyl)pyrazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-3-(methoxymethyl)-1-{2'-methyl-1',3'-dihydrospiro[cyclopropane-1,4'-isoquinoline]-7'-ylmethyl}pyrazole-4-carboxamide;

1-{2',3'-dihydro-1'H-spiro[cyclopropane-1,4'-isoquinoline]-7'-ylmethyl}-N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-3-(methoxymethyl)pyrazole-4-carboxamide;

3-(difluoromethyl)-N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-1-({5-methyl-4H,6H,7H-pyrazolo[1,5-a]pyrazin-2-yl}methyl)pyrazole-4-carboxamide;

3-(difluoromethyl)-N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-1-[(7-methyl-6,8-dihydro-5H-1,7-naphthyridin-3-yl)methyl]pyrazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]-1,2,3-triazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-1-[(2-isopropyl-1,3-dihydroisoindol-5-yl)methyl]-1,2,3-triazole-4-carboxamide;

N-({2-chloro-6-[3-(difluoromethyl)-1,2,4-triazol-1-yl]-3-methoxyphenyl}methyl)-3-(methoxymethyl)-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]pyrazole-4-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-1-[(2-methyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]-6-oxopyridine-3-carboxamide;

N-{[2-fluoro-3-methoxy-6-(4-methyl-1,2,3-triazol-1-yl)phenyl]methyl}-5-[(2-methyl-3,4-dihydro-1H-isoquinolin-7-yl)methyl]pyridine-3-carboxamide;

and pharmaceutically acceptable salts and/or solvates thereof.

9. A compound, as claimed in any of claims 1 to 8, or a pharmaceutically acceptable salt, solvate, or solvate of a salt thereof.

10. A pharmaceutical composition comprising:

(i) a compound , or a pharmaceutically acceptable salt, or a pharmaceutically acceptable solvate thereof, or a pharmaceutically acceptable solvate of a salt thereof as claimed in claim 9; and

(ii) a pharmaceutically acceptable carrier, diluent or excipient.

11. A compound as claimed in claim 9, or the pharmaceutical composition as claimed in claim 10, for use in medicine.

12. Use of a compound as claimed in claim 9, or a pharmaceutical composition as claimed in claim 10, in the manufacture of a medicament for the treatment of a disease or condition in which plasma kallikrein activity is implicated.

13. The use of a compound or a pharmaceutical composition as claimed in claim 12, wherein, the disease or condition in which plasma kallikrein activity is implicated is a bradykinin-mediated angioedema, optionally,

(i) wherein the bradykinin-mediated angioedema is hereditary angioedema, or

(ii) wherein the bradykinin-mediated angioedema is non hereditary, or

(iii) wherein the bradykinin-mediated angioedema is hereditary angioedema or an acute non-hereditary bradykinin-mediated angioedema.

14. The use of a compound or a pharmaceutical composition as claimed in claim 12, wherein the disease or condition in which plasma kallikrein activity is implicated is selected from impaired visual acuity, diabetic retinopathy, diabetic macular edema, diabetes, pancreatitis, cerebral haemorrhage, nephropathy, cardiomyopathy, neuropathy, inflammatory bowel disease, arthritis, inflammation, septic shock, hypotension, cancer, adult respiratory distress syndrome, disseminated intravascular coagulation, cardiopulmonary bypass surgery and bleeding from post operative surgery.