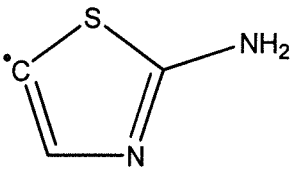
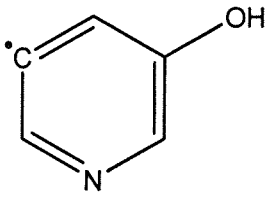


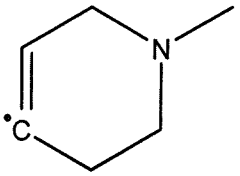
3-fluoro-5-hydroxyphenyl



2-amino-1,3-thiazol-5-yl



5-hydroxypyridin-3yl



1-methyl-1,2,3,6-tetrahydropyridin-4yl

In one embodiment:

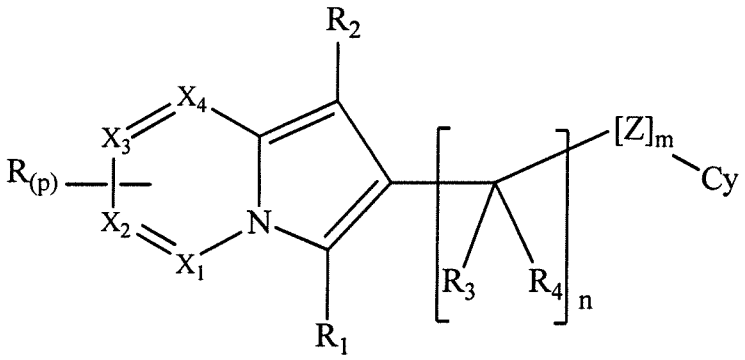
X_1, X_2, X_3 and X_4 are all CH groups;

R is selected from the group consisting of C_1-C_6 alkyl, such as methyl, C_1-C_6 haloalkyl such as trifluoromethyl, and halogen, more preferably fluoro, chloro and bromo;

R_1 is selected in the group consisting of hydrogen, C_2-C_6 alkynyl such as 3-pent-1-yn-1-yl, C_2-C_6 aminoalkynyl such as 3-dimethylaminoprop-1-yn-1-yl, and C_2-C_6 hydroxyalkynyl such as 3-hydroxyprop-1-yn-1-yl, aryl, such as phenyl, heteroaryl, such as pyridyl, pyrazinyl, thienyl and thiazolyl, C_3-C_6 heterocycloalkyl such as 3,6-dihydro-2H-pyran-4-yl, 1,2,3,6-tetrahydropyridin-4-yl, pyrrolidin-1-yl-2-one, and 4-methylpiperazin-1-yl-2-one, a group -$(CH_2)_nNR_{22}R_{23}$ such as 4-morpholinomethyl, 2-methyl-2,9-diazaspiro[5.5]undecan-9-ylmethyl, 9-methyl-3,9-diazaspiro[5.5]undecan-3-yl}methyl, 7-methyl-2,7-diazaspiro[3.5]nonan-2-yl}methyl, and 5-methyl-octahydropyrrolo[3,4-c]pyrrol-2-yl]methyl, wherein each aryl and heteroaryl may be optionally substituted by one or two groups independently selected from halogen such as chlorine and fluorine, cyano, (C_1-C_6) alkyl such as methyl, -$C(O)NR_{12}R_{13}$ such as 4-morpholinocarbonyl, (C_3-C_6) heterocycloalkyl such as 1-methylpyrrolidin-1-yl, -$NR_{22}R_{23}$ such as dimethylamino, -$(CH_2)_nNR_{22}R_{23}$ such as 2-dimethylaminomethyl, N,N-bis(2-hydroxyethyl)amino, 4-morpholinomethyl, 2-(4-morpholino)ethyl, 1-pyrrolidinomethyl, and (4-methylpiperazin-

CLAIMS

1. A compound of formula (I)



(I)

wherein

X_1, X_2, X_3 and X_4 are all CH groups;

each **R**, when present, is selected from the group consisting of halogen, (C_1-C_6) alkyl and (C_1-C_6) haloalkyl;

R_1 is selected from the group consisting of -H, -OR_6, -SR_6, -$S(O)_q$-R_8, halogen, -$NR_{12}R_{13}$, -CN, -$C(O)NR_{12}R_{13}$, -$C(O)OR_{16}$, (C_1-C_6) alkyl, (C_1-C_6) haloalkyl, (C_1-C_6) hydroxyalkyl, (C_1-C_6) aminoalkyl, (C_3-C_7) cycloalkyl, (C_2-C_6) alkenyl, (C_5-C_7) cycloalkenyl, (C_2-C_6) alkynyl, (C_2-C_6) hydroxyalkynyl, and by a group selected from aryl, heteroaryl and (C_3-C_6) heterocycloalkyl; each of which being in his turn optionally and independently substituted with one or more groups selected from halogen, -$NR_{22}R_{23}$, -$(CH_2)_nNR_{22}R_{23}$, (C_1-C_6) alkyl, (C_1-C_6) alkoxyl, (C1-C6) aminoalkoxyl (C_3-C_6) heterocycloalkyloxyl or (C_3-C_6) heterocycloalkyl (C_1-C_6) alkoxyl, (C_1-C_6) haloalkyl, (C_1-C_6) hydroxyalkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, (C_2-C_6) hydroxyalkynyl;

R_2 is selected from the group consisting of -H, -OR_9, -SR_9, -$S(O)_q$-R_{17}, halogen, -$NR_{14}R_{15}$, -CN, -$C(O)NR_{14}R_{15}$, -$C(O)OR_{18}$, -(C_1-C_6) alkyl, -(C_1-C_6) haloalkyl, -(C_1-C_6) hydroxyalkyl, (C_1-C_6) aminoalkyl, (C_3-C_7) cycloalkyl, (C_5-C_7) cycloalkenyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, (C_2-C_6) hydroxyalkynyl, and by a group selected from aryl, heteroaryl and (C_3-C_6) heterocycloalkyl; each of which being in his turn optionally and independently substituted with one or more groups selected from halogen; -$NR_{24}R_{25}$, -

$(CH_2)_nNR_{24}R_{25}$, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ haloalkyl, $(C_1\text{-}C_6)$ hydroxyalkyl, $(C_2\text{-}C_6)$ alkenyl, $(C_2\text{-}C_6)$ alkynyl, $(C_2\text{-}C_6)$ hydroxyalkynyl ;

R_3 is selected from –H and $(C_1\text{-}C_6)$ alkyl;

R_4 is H;

Cy is an heteroaryl selected from the group consisting of I-1 to I-5 wherein (I-1) is 3H-purin-3-yl, (I-2) is 9H-purin-9-yl, (I-3) is 9H-purin-6-yl, (I-4) is 1H-pyrazolo[3,4-d]pyrimidin-1-yl, (I-5) is 6-oxo-5H-,6H,7H-pyrrolo[2,3-d]pyrimidin4-yl; each of which being optionally and independently substituted by one or more groups selected from halogen, -OH, $-NR_{19}R_{20}$, $-CH_2NR_{19}R_{20}$; -CN, -CH(O), -CH=NOH, $-C(O)NR_{19}R_{20}$, $-C(O)OR_{21}$, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ haloalkyl, $(C_1\text{-}C_6)$ hydroxyalkyl, $(C_2\text{-}C_6)$ alkenyl, $(C_2\text{-}C_6)$ alkynyl, $(C_2\text{-}C_6)$ hydroxyalkynyl, or by a group selected from aryl, heteroaryl and $(C_3\text{-}C_6)$ heterocycloalkyl, each of which being in his turn optionally and independently substituted with one or more groups selected from –OH, halogen, -CN, $-S(O)_2NR^IR^{III}$, - $NR^{III}S(O)_2R^{II}$, $-NR^IR^{III}$, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ haloalkyl, $(C_1\text{-}C_6)$ hydroxyalkyl, $(C_1\text{-}C_6)$alkoxy, aryl, heteroaryl, $(C_3\text{-}C_6)$ heterocycloalkyl;

wherein R^I R^{II} and R^{III} the same or different, are independently selected from the group consisting of –H, $(C_1\text{-}C_6)$ alkyl and alkanoyl;

R_5, R_6, R_9, R_{16}, R_{18}, and R_{21} the same or different, are independently selected from the group consisting of -H, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ haloalkyl, $(C_1\text{-}C_6)$ hydroxyalkyl, $(C_1\text{-}C_6)$ aminoalkyl, alkanoyl, and aryl alkanoyl;

R_7, R_8 and R_{17}, the same or different, are independently selected from the group consisting of $NR_{12}R_{13}$, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ haloalkyl, $(C_1\text{-}C_6)$ hydroxyalkyl, $(C_1\text{-}C_6)$ aminoalkyl, or by a group selected from aryl, heteroaryl and $(C_3\text{-}C_6)$ heterocycloalkyl each of which being in his turn optionally and independently substituted with one or more groups selected from halogen, $-NR_{22}R_{23}$, $-CH_2NR_{22}R_{23}$, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ haloalkyl, $(C_1\text{-}C_6)$ hydroxyalkyl, $(C_2\text{-}C_6)$ alkenyl, $(C_2\text{-}C_6)$ alkynyl, $(C_2\text{-}C_6)$ hydroxyalkynyl;

R_{10}, R_{11}, R_{12}, R_{13}, R_{14}, R_{15}, R_{19}, R_{20}, R_{22}, R_{23}, R_{24} and R_{25}, the same or different, are independently selected from the group consisting of –H, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ hydroxyalkyl and alkanoyl or, taken together with the nitrogen atom they are linked to, anyone of R_{10} and R_{11}, R_{12} and R_{13}, R_{14} and R_{15}, R_{19} and R_{20}, R_{22} and R_{23}, R_{24} and R_{25}

may form, a 5 to 6 membered heterocycle optionally containing one additional heteroatom selected from O, S, N;

Z is either absent or -NH-;

m is zero or 1;

n is 1 or 2,

p is zero or an integer ranging from 1 to 3

q is an integer ranging from 1 to 2

or pharmaceutically acceptable salts thereof.

2. A compound according to Claim 1 present as a mixture of diastereoisomers.

3. A compound according to Claims 1 or 2 wherein:

R_3 is selected from H and (C_1-C_6) alkyl;

R_4 is H;

R, R_1, R_2, m, n, p, Z, Cy and X_{1-4} are as defined in claim 1 or pharmaceutically acceptable salt thereof.

4. A compound according to any of claims 1 to 3 wherein:

R_3 is methyl;

R_4 is H;

Cy is 1H-pyrazolo[3,4-d]pyrimidin-1-yl (I-4), which is optionally and independently substituted by one or more groups selected from $-NR_{19}R_{20}$ and aryl which is optionally substituted by one or more groups selected from OH and halogen; all the other variables being as defined in claim 1,

or pharmaceutically acceptable salt thereof.

5. A compound according to claim 4 wherein:

R_1 is selected from the group consisting of 4-morpholinomethyl, 2-methyl-2,9-diazaspiro[5.5]undecan-9-yl}methyl, 9-methyl-3,9-diazaspiro[5.5]undecan-3-yl}methyl, 7-methyl-2,7-diazaspiro[3.5]nonan-2-yl}methyl, and 5-methyl-octahydropyrrolo[3,4-c]pyrrol-2-yl]methyl;

R_3 is methyl;

R_4 is H;

Cy is 1H-pyrazolo[3,4-d]pyrimidin-1-yl (I-4), which is substituted in the position 4 by $-NH_2$ and in the position 3 by 3-fluoro-5-hydroxyphenyl; all the other variables being as defined in claim 1.

or pharmaceutically acceptable salt thereof.

6. A compound according to claim 1, wherein:

R is selected from the group consisting of methyl, trifluoromethyl, fluoro, chloro and bromo;

R_1 is selected in the group consisting of hydrogen, C_2-C_6 alkynyl such as 3-pent-1-yn-1-yl, C_2-C_6 aminoalkynyl such as 3-dimethylaminoprop-1-yn-1-yl, and C_2-C_6 hydroxyalkynyl such as 3-hydroxyprop-1-yn-1-yl, aryl, such as phenyl, heteroaryl, such as pyridyl, pyrazinyl, thienyl and thiazolyl, C_3-C_6 heterocycloalkyl such as 3,6-dihydro-2H-pyran-4-yl, 1,2,3,6-tetrahydropyridin-4-yl, pyrrolidin-1-yl-2-one, and 4-methylpiperazin-1-yl-2-one, a group $-(CH_2)_nR_{22}R_{23}$ such as 4-morpholinomethyl, 2-methyl-2,9-diazaspiro[5.5]undecan-9-ylmethyl, 9-methyl-3,9-diazaspiro[5.5]undecan-3-yl}methyl, 7-methyl-2,7-diazaspiro[3.5]nonan-2-yl}methyl, and 5-methyl-octahydropyrrolo[3,4-c]pyrrol-2-yl]methyl, wherein each aryl and heteroaryl may be optionally substituted by one or two groups independently selected from halogen such as chlorine and fluorine, cyano, (C_1-C_6) alkyl such as methyl, $-C(O)NR_{12}R_{13}$ such as 4-morpholinocarbonyl, (C_3-C_6) heterocycloalkyl such as 1-methylpyrrolidin-1-yl, $-NR_{22}R_{23}$ such as dimethylamino, $-(CH_2)_nNR_{22}R_{23}$ such as 2-dimethylaminomethyl, N,N-bis(2-hydroxyethyl)amino, 4-morpholinomethyl, 2-(4-morpholino)ethyl, 1-pyrrolidinomethyl, and (4-methylpiperazin-1-yl)methyl, (C_3-C_6) heterocycloalkoxyl such as 1-methylpiperidin-4-yl-oxyl, (C_3-C_6) heterocycloalkyl (C_1-C_6) alkoxyl such as 2-(4-methylpiperazin-1yl)ethoxyl, 2-(4-morpholino)ethoxyl, 2-dimethylaminoethoxyl and 2-(1-methylpiperidin-4-yl)ethoxyl;

R_2 is selected in the group consisting of hydrogen, cyano, (C_1-C_6) haloalkyl such as trifluoromethyl, aryl such as phenyl which is optionally substituted by halogen such as fluoro and methyl, heteroaryl such as pyridinyl;

R_3 is selected from the group consisting of H and (C_1-C_6) alkyl such as methyl

and ethyl;

R_4 is H;

Cy is an heteroaryl selected from the following group: 9H-purine-6-amine-9-yl, 3H-purine-6-amine-3-yl, 9H-purin-6-yl, 4-amino-3-(3-fluoro-5-methoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-acetylaminophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-hydroxymethylphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(5-hydroxy-3-trifluoromethylphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-fluorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-methanesulphonylaminophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-pyridyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(5-hydroxy-3-pyridyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-fluoro-4-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(4-fluoro-3-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-chloro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-aminosulphonylphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-sulphonylamino-5-fluorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-aminosulphonyl-5-fluorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-amino-5-fluorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-cyano-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-fluoro-5-(1H-1,2,3,4-tetrazol-5-yl)phenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-hydroxypropyn-1-yl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, and 4-amino-3-(2-aminothiazol-5-yl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl.

m is 1;

n is 1;

p is 1;

and all the other variables are as defined in claim 1.

7. A compound according to claim 6, wherein:

R_1 is selected in the group consisting of hydrogen, C_2-C_6 alkynyl which is 3-pent-1-yn-1-yl, C_2-C_6 aminoalkynyl which is 3-dimethylaminoprop-1-yn-1-yl, and C_2-C_6 hydroxyalkynyl which is 3-hydroxyprop-1-yn-1-yl, aryl which is phenyl, heteroaryl

selected from pyridyl, pyrazinyl, thienyl and thiazolyl, C_3-C_6 heterocycloalkyl selected from 3,6-dihydro-2H-pyran-4-yl, 1,2,3,6-tetrahydropyridin-4-yl, pyrrolidin-1-yl-2-one, and 4-methylpiperazin-1-yl-2-one, a group $-(CH_2)_nN_{22}N_{23}$ selected from 4-morpholinomethyl, 2-methyl-2,9-diazaspiro[5.5]undecan-9-ylmethyl, 9-methyl-3,9-diazaspiro[5.5]undecan-3-yl}methyl, 7-methyl-2,7-diazaspiro[3.5]nonan-2-yl}methyl, and 5-methyl-octahydropyrrolo[3,4-c]pyrrol-2-yl]methyl, wherein each aryl and heteroaryl may be optionally substituted by one or two groups independently selected from halogen selected from chlorine and fluorine, cyano, (C_1-C_6) alkyl which is methyl, $-C(O)NR_{12}R_{13}$ which is 4-morpholinocarbonyl, (C_3-C_6) heterocycloalkyl which is 1-methylpyrrolidin-1-yl, $-NR_{22}R_{23}$ which is dimethylamino, $-(CH_2)_nNR_{22}R_{23}$ selected from 2-dimethylaminomethyl, N,N-bis(2-hydroxyethyl)amino, 4-morpholinomethyl, 2-(4-morpholino)ethyl, 1-pyrrolidinomethyl, and (4-methylpiperazin-1-yl)methyl, (C_3-C_6) heterocycloalkoxyl which is 1-methylpiperidin-4-yl-oxyl, (C_3-C_6) heterocycloalkyl (C_1-C_6) alkoxyl selected from 2-(4-methylpiperazin-1yl)ethoxyl, 2-(4-morpholino)ethoxyl, 2-dimethylaminoethoxyl and 2-(1-methylpiperidin-4-yl)ethoxyl;

R_2 is selected in the group consisting of hydrogen, cyano, (C_1-C_6) haloalkyl which is trifluoromethyl, aryl which is phenyl which is optionally substituted by halogen which is fluoro or methyl, heteroaryl which is pyridinyl;

R_3 is selected from the group consisting of H and (C_1-C_6) alkyl selected from methyl and ethyl;

R_4 is H;

Cy is an heteroaryl selected from the following group: 9H-purine-6-amine-9-yl, 3H-purine-6-amine-3-yl, 9H-purin-6-yl, 4-amino-3-(3-fluoro-5-methoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-acetylaminophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-hydroxymethylphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(5-hydroxy-3-trifluoromethylphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-fluorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-methanesulphonylaminophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-pyridyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl,
4-amino-3-(5-hydroxy-3-pyridyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-fluoro-4-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(4-fluoro-3-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-chloro-5-

hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-aminosulphonylphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-sulphonylamino-5-fluorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-aminosulphonyl-5-fluorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-amino-5-fluorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-cyano-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-fluoro-5-(1H-1,2,3,4-tetrazol-5-yl)phenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, 4-amino-3-(3-hydroxypropyn-1-yl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl, and 4-amino-3-(2-aminothiazol-5-yl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl.

m is 1;

n is 1;

p is 1;

Z is absent or is selected from –NH- or -NHC(O)-;

and all the other variables are as defined in claim 1.

8. A compound according to Claim 1 selected from:

9-[(3-phenylindolizin-2-yl)methyl]-9H-purin-6-amine,

3-[(3-phenylindolizin-2-yl)methyl]-3H-purin-6-amine,

9-{[3-(pyridin-2-yl)indolizin-2-yl]methyl}-9H-purin-6-amine,

9-{[3-(3-fluorophenyl)indolizin-2-yl]methyl}-9H-purin-6-amine,

3-{[3-(3-fluorophenyl)indolizin-2-yl]methyl}-3H-purin-6-amine,

9-{[3-(2-fluorophenyl)indolizin-2-yl]methyl}-9H-purin-6-amine,

9-{[3-(2-methylphenyl)indolizin-2-yl]methyl}-9H-purin-6-amine,

3-{[3-(2-methylphenyl)indolizin-2-yl]methyl}-3H-purin-6-amine,

9-(indolizin-2-ylmethyl)-9H-purin-6-amine,

9-[(1-phenylindolizin-2-yl)methyl]-9H-purin-6-amine,

9-{[1-(3-fluorophenyl)indolizin-2-yl]methyl}-9H-purin-6-amine,

9-{[1-(2-methylphenyl)indolizin-2-yl]methyl}-9H-purin-6-amine,

N-[(3-phenylindolizin-2-yl)methyl]-9H-purin-6-amine,

N-{[3-(pyridin-2-yl)indolizin-2-yl]methyl}-9H-purin-6-amine,

N-{[3-(3-fluorophenyl)indolizin-2-yl]methyl}-9H-purin-6-amine,

N-{[3-(2-fluorophenyl)indolizin-2-yl]methyl}-9H-purin-6-amine,
N-[(1-phenylindolizin-2-yl)methyl]-9H-purin-6-amine,
N-{[1-(3-fluorophenyl)indolizin-2-yl]methyl}-9H-purin-6-amine,
N-{[1-(2-methylphenyl)indolizin-2-yl]methyl}-9H-purin-6-amine,
N-{[1-(pyridin-2-yl)indolizin-2-yl]methyl}-9H-purin-6-amine,
N-(indolizin-2-ylmethyl)-9H-purin-6-amine,
3-phenyl-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-4-amine,
3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)phenol,
3-(3-fluoro-5-methoxyphenyl)-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-4-amine,
N-[3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)phenyl]acetamide,
[3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)phenyl]methanol,
3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-(trifluoromethyl)phenol,
3-(3-fluorophenyl)-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-4-amine,
N-[3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)phenyl]methanesulfonamide,
1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-3-(pyridin-3-yl)-1H-pyrazolo[3,4-d]pyrimidin-4-amine,
5-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)pyridin-3-ol,
4-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-2-fluorophenol,
5-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-2-fluorophenol,
3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-chlorophenol,

3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)benzene-1-sulfonamide,

N-[3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenyl]methanesulfonamide,

3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorobenzene-1-sulfonamide,

3-(3-amino-5-fluorophenyl)-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-4-amine,

3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-hydroxybenzonitrile,

3-[3-fluoro-5-(1H-1,2,3,4-tetrazol-5-yl)phenyl]-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-4-amine,

3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol enantiomer 1,

3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol enantiomer 2,

3-(4-amino-1-{1-[3-(pyridin-4-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-{4-amino-1-[1-(3-phenylindolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,

3-(4-amino-1-{1-[3-(2-fluorophenyl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluoro-phenol,

3-(4-amino-1-{1-[6-methyl-3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{1-[3-(pyridin-2-yl)-6-(trifluoromethyl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{1-[1-methyl-3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-[4-amino-1-(1-{3-[5-(morpholin-4-ylmethyl)thiophen-2-yl]indolizin-2-yl}ethyl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-5-fluorophenol,

3-{4-amino-1-[1-(3-{4-[(dimethylamino)methyl]phenyl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,

3-{4-amino-1-[1-(3-{3-[(dimethylamino)methyl]phenyl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,

3-{4-amino-1-[1-(3-{3-[(dimethylamino)methyl]phenyl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol enantiomer 1,

3-{4-amino-1-[1-(3-{3-[(dimethylamino)methyl]phenyl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol enantiomer 2,

3-(4-amino-1-{1-[3-(1,3-thiazol-5-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

1-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)pyrrolidin-2-one,

3-(4-amino-1-{1-[7-(pyridin-2-yl)pyrrolo[1,2-b]pyridazin-6-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{[3-(pyridin-2-yl)indolizin-2-yl]methyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{[3-(pyridin-3-yl)indolizin-2-yl]methyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{[3-(pyridin-4-yl)indolizin-2-yl]methyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{[7-(pyridin-2-yl)pyrrolo[1,2-b]pyridazin-6-yl]methyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{1-[3-(1,2,3,6-tetrahydropyridin-4-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)prop-2-yn-1-ol,

5-(4-amino-1-{1-[3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-1,3-thiazol-2-amine,

3-(4-amino-1-{1-[7-chloro-3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{1-[7-methyl-3-(pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{1-[3-(2-methylpyridin-4-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

5-(4-amino-1-{1-[3-(2-methylpyridin-4-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)pyridin-3-ol,

3-[4-amino-1-(1-{3-[5-(morpholin-4-ylmethyl)pyridin-2-yl]indolizin-2-yl}ethyl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-5-fluorophenol,

3-[4-amino-1-(1-{3-[5-(morpholin-4-ylmethyl)pyridin-2-yl]indolizin-2-yl}ethyl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-5-fluorophenol enantiomer 1,

3-[4-amino-1-(1-{3-[5-(morpholin-4-ylmethyl)pyridin-2-yl]indolizin-2-yl}ethyl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-5-fluorophenol enantiomer 2,

3-{4-amino-1-[1-(3-{5-[(dimethylamino)methyl]pyridin-2-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,

3-[4-amino-1-(1-{3-[6-(morpholin-4-ylmethyl)pyridin-2-yl]indolizin-2-yl}ethyl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-5-fluorophenol,

3-[4-amino-1-(1-{3-[4-(morpholin-4-ylmethyl)pyridin-2-yl]indolizin-2-yl}ethyl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-5-fluorophenol,

3-{4-amino-1-[1-(3-{4-[(dimethylamino)methyl]pyridin-2-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,

3-[4-amino-1-(1-{3-[5-(pyrrolidin-1-ylmethyl)pyridin-2-yl]indolizin-2-yl}ethyl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-5-fluorophenol,

3-{4-amino-1-[1-(3-{5-[(4-methylpiperazin-1-yl)methyl]pyridin-2-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,

3-{4-amino-1-[1-(3-{5-[(4-methylpiperazin-1-yl)methyl]pyridin-2-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol enantiomer 1,

3-{4-amino-1-[1-(3-{5-[(4-methylpiperazin-1-yl)methyl]pyridin-2-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol enantiomer 2,

3-{4-amino-1-[1-(3-{6-[(4-methylpiperazin-1-yl)methyl]pyridin-2-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,

3-{4-amino-1-[1-(3-{4-[(4-methylpiperazin-1-yl)methyl]pyridin-2-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,

3-(4-amino-1-{1-[3-(5-{[bis(2-hydroxyethyl)amino]methyl}pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,

3-(4-amino-1-{1-[3-(5-{[bis(2-hydroxyethyl)amino]methyl}pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol enantiomer 1,
3-(4-amino-1-{1-[3-(5-{[bis(2-hydroxyethyl)amino]methyl}pyridin-2-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol enantiomer 2,
3-[4-amino-1-(1-{3-[3-(1-methylpyrrolidin-2-yl)phenyl]indolizin-2-yl}ethyl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-5-fluorophenol,
3-{4-amino-1-[1-(3-{5-[2-(morpholin-4-yl)ethoxy]pyridin-2-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,
5-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-1-[2-(morpholin-4-yl)ethyl]-1,2-dihydropyridin-2-one,
4-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-1-[2-(morpholin-4-yl)ethyl]-1,2-dihydropyridin-2-one,
4-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-1-[2-(morpholin-4-yl)ethyl]-1,2-dihydropyridin-2-one enantiomer 1,
4-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-1-[2-(morpholin-4-yl)ethyl]-1,2-dihydropyridin-2-one enantiomer 2,
4-(2-{1-[4-amino-3-(5-hydroxypyridin-3-yl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-1-[2-(morpholin-4-yl)ethyl]-1,2-dihydropyridin-2-one;
2-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)benzonitrile,
3-(4-amino-1-{1-[3-(pyridin-2-yl)-1-(trifluoromethyl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,
3-[4-amino-1-(1-{3-[5-(morpholine-4-carbonyl)pyridin-2-yl]indolizin-2-yl}ethyl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-5-fluorophenol,
2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}-3-(pyridin-2-yl)indolizine-1-carbonitrile,
2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}-3-{3-[(dimethylamino)methyl]phenyl}indolizine-1-carbonitrile,
2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}-3-{3-[(dimethylamino)methyl]phenyl}indolizine-1-carbonitrile enantiomer 1,

2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}-3-{3-[(dimethylamino)methyl]phenyl}indolizine-1-carbonitrile enantiomer 2,
3-{4-amino-1-[1-(7-{3-[(dimethylamino)methyl]phenyl}pyrrolo[1,2-b]pyridazin-6-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,
3-(4-amino-1-{1-[3-(1,3-thiazol-4-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,
3-[4-amino-1-(1-{3-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]indolizin-2-yl}ethyl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-5-fluorophenol,
3-[4-amino-1-(1-{3-[3-(dimethylamino)prop-1-yn-1-yl]indolizin-2-yl}ethyl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-5-fluorophenol,
1-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-4-methylpiperazin-2-one,
4-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-1-[2-(dimethylamino)ethyl]-1,2-dihydropyridin-2-one,
4-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-1-[2-(dimethylamino)ethyl]-1,2-dihydropyridin-2-one enantiomer 1,
4-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-1-[2-(dimethylamino)ethyl]-1,2-dihydropyridin-2-one enantiomer 2,
6-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-2-[2-(pyrrolidin-1-yl)ethyl]-2,3-dihydropyridazin-3-one,
6-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-2-[2-(4-methylpiperazin-1-yl)ethyl]-2,3-dihydropyridazin-3-one,
6-(2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}indolizin-3-yl)-2-[2-(morpholin-4-yl)ethyl]-2,3-dihydropyridazin-3-one,
3-{4-amino-1-[1-(3-{6-[2-(4-methylpiperazin-1-yl)ethoxy]pyridazin-3-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,
3-{4-amino-1-[1-(3-{6-[2-(dimethylamino)ethoxy]pyridazin-3-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,
3-{4-amino-1-[1-(3-{6-[(1-methylpiperidin-4-yl)oxy]pyridazin-3-yl}indolizin-2-

yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,
3-{4-amino-1-[1-(3-{6-[2-(1-methylpiperidin-4-yl)ethoxy]pyridazin-3-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,
3-(4-amino-1-{1-[3-(morpholin-4-ylmethyl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,
3-(4-amino-1-{1-[3-({2-methyl-2,9-diazaspiro[5.5]undecan-9-yl}methyl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,
3-(4-amino-1-{1-[3-({9-methyl-3,9-diazaspiro[5.5]undecan-3-yl}methyl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,
3-(4-amino-1-{1-[3-({7-methyl-2,7-diazaspiro[3.5]nonan-2-yl}methyl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,
3-{1-[1-(3-{[(3aR,6aS)-5-methyl-octahydropyrrolo[3,4-c]pyrrol-2-yl]methyl}indolizin-2-yl)ethyl]-4-amino-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,
2-{1-[4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]ethyl}-3-(morpholin-4-ylmethyl)indolizine-1-carbonitrile,
3-{4-amino-1-[1-(3-{1-[2-(dimethylamino)ethyl]-1H-pyrazol-3-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,
3-{4-amino-1-[1-(3-{1-[2-(4-methylpiperazin-1-yl)ethyl]-1H-pyrazol-3-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,
3-(4-amino-1-{1-[3-(1-{2-[bis(2-hydroxyethyl)amino]ethyl}-1H-pyrazol-3-yl)indolizin-2-yl]ethyl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-5-fluorophenol,
3-{4-amino-1-[1-(3-{1-[2-(morpholin-4-yl)ethyl]-1H-pyrazol-3-yl}indolizin-2-yl)ethyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-5-fluorophenol,
and pharmaceutically acceptable salt thereof.

9. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, either alone or in combination with one or more active ingredient, in admixture with one or more pharmaceutically acceptable carrier or excipient.

10. A compound according to any one of claims 1 to 8 for use as a medicament.

11. A compound for use according to claim 10, for use in the treatment of a disorder associated by PI3K enzymes mechanisms that is selected from the group consisting of respiratory diseases selected from idiopathic chronic cough, cough variant asthma, cough associated with thoracic tumour or lung cancer, viral or post-viral cough, upper airways cough syndrome or post nasal drip cough, or cough associated gastro oesophageal acid and non-acid reflux disease, chronic bronchitis, chronic obstructive pulmonary disease, interstitial lung disease selected from idiopathic pulmonary fibrosis, congestive heart disease, sarcoidosis or whooping cough and asthma; viral infections selected from viral respiratory tract infections and viral exacerbation of respiratory diseases selected from asthma and chronic obstructive pulmonary disease; non-viral respiratory infections selected from aspergillosis and leishmaniasis; allergic diseases selected from allergic rhinitis and atopic dermatitis; autoimmune diseases selected from rheumatoid arthritis and multiple sclerosis; inflammatory disorders selected from inflammatory bowel disease; cardiovascular diseases selected from thrombosis and atherosclerosis; hematologic malignancies; neurodegenerative diseases; pancreatitis; multiorgan failure; kidney diseases; platelet aggregation; cancer; sperm motility; transplantation rejection; graft rejection; lung injuries; and pain selected from pain associated with rheumatoid arthritis or osteoarthritis, back pain, general inflammatory pain, post hepatic neuralgia, diabetic neuropathy, inflammatory neuropathic pain (trauma), trigeminal neuralgia, central pain and respiratory infections, airways damage, treatment and/or prevention of airway injury in patients with PI3Kδ mutations.

12. A compound for use according to claim 11 wherein the disorder associated by PI3K enzymes mechanisms is asthma, chronic obstructive pulmonary disease or idiopathic pulmonary fibrosis.

13. Use of a compound as defined in any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a disorder associated by PI3K enzymes mechanisms that is selected from the group consisting of respiratory diseases selected from idiopathic chronic cough, cough variant asthma, cough associated with thoracic tumour or lung cancer, viral or post-viral cough, upper airways cough syndrome or post nasal drip cough, or cough associated gastro

oesophageal acid and non-acid reflux disease, chronic bronchitis, chronic obstructive pulmonary disease, interstitial lung disease selected from idiopathic pulmonary fibrosis, congestive heart disease, sarcoidosis or whooping cough and asthma; viral infections selected from viral respiratory tract infections and viral exacerbation of respiratory diseases selected from asthma and chronic obstructive pulmonary disease; non-viral respiratory infections selected from aspergillosis and leishmaniasis; allergic diseases selected from allergic rhinitis and atopic dermatitis; autoimmune diseases selected from rheumatoid arthritis and multiple sclerosis; inflammatory disorders selected from inflammatory bowel disease; cardiovascular diseases selected from thrombosis and atherosclerosis; hematologic malignancies; neurodegenerative diseases; pancreatitis; multiorgan failure; kidney diseases; platelet aggregation; cancer; sperm motility; transplantation rejection; graft rejection; lung injuries; and pain selected from pain associated with rheumatoid arthritis or osteoarthritis, back pain, general inflammatory pain, post hepatic neuralgia, diabetic neuropathy, inflammatory neuropathic pain (trauma), trigeminal neuralgia, central pain and respiratory infections, airways damage, treatment and/or prevention of airway injury in patients with PI3Kδ mutations.

14. Use according to claim 13 wherein the disorder associated by PI3K enzymes mechanisms is asthma, chronic obstructive pulmonary disease or idiopathic pulmonary fibrosis.