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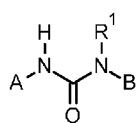
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(I)

(57) Abstract: The present invention covers urea compounds of general formula (I) in which R¹, A and B are as defined herein, methods of preparing said compounds, intermediate compounds useful for preparing said compounds, pharmaceutical compositions and combinations comprising said compounds and the use of said compounds for manufacturing pharmaceutical compositions for the treatment or prophylaxis of diseases, in particular of hyperproliferative disorders, as a sole agent or in combination with other active ingredients.



UREA DERIVATIVES

The present invention covers urea compounds of general formula (I) as described and defined herein, methods of preparing said compounds, and the use of said compounds for manufacturing pharmaceutical compositions for the treatment or prophylaxis of diseases, in particular of cancer disorders, as a sole agent or in combination with other active ingredients.

BACKGROUND

The present invention covers urea compounds of general formula (I) which inhibit the function of SWI/SNF complex core component SMARCA2.

Cancer is among the leading causes of mortality worldwide and it was predicted that in 2018; 1,735,350 new cancer cases and 609,640 cancer deaths will occur in the United States. These high numbers are expected to further rise in the future, primarily due to the increasing size and the ageing of world's population. Although the survival rates of many cancer types improved over the last decades, the most metastatic and late stage diseases still remained very difficult to control; therefore there is a need for novel therapeutics in nearly every cancer indication.

Cancer is caused by genetic and epigenetic alterations, which affect the gene expression programs or the signaling pathways of normal cells, ultimately leading to their transformation into malignant cancer cells. Recent cancer genome sequencing efforts on tumor samples have revealed that ATP-dependent chromatin remodelers are frequently mutated across different cancer types. SWI/SNF complex is one of the four distinct families of the human ATP-dependent remodelers of chromatin structure, and genes encoding for its subunits have been found to be mutated in more than 20% of all human cancers. The majority of these mutations are loss-of-function, suggesting that the subunits of SWI/SNF complex play tumor suppressor roles and therefore such cancers remain a therapeutic challenge.

The multisubunit SWI/SNF complex is comprised of several chromatin binding subunits and of one of two mutually exclusive ATPase paralogues; SMARCA2 or SMARCA4. ATP hydrolysis by one of these two core enzymes provide the complex with the energy required for nucleosome sliding, eviction and replacement, thereby controlling gene expression and other key cellular processes.

SMARCA4 is one of the most frequently inactivated, or epigenetically silenced, subunits of the SWI/SNF complex across diverse cancer types including, but not limited to, lung cancer, colorectal cancer, gastric cancer, esophageal cancer, bladder cancer, liver cancer, cervical cancer, breast cancer, ovarian cancer and other cancer types. In contrast, SMARCA2 is rarely mutated, and in certain conditions, due to functional redundancy, SMARCA2 can compensate for the loss of SMARCA4 and sustain the SWI/SNF complex functionality to support cell viability. Therefore the survival of SMARCA4-deficient cancer cells strongly depends on the function of SMARCA2. In line with this, genome-wide screening efforts revealed that down-regulation of SMARCA2 in SMARCA4-deficient, but not in SMARCA4-proficient genetic backgrounds, results in strong synthetic lethality mediated by G1 arrest and induction of senescence (Oike T et al., 2013, Cancer Res; Hoffman GR et al., 2014, Proc Natl Acad Sci USA; Wilson BG et al., 2014, Mol Cell Biol;). This synthetic lethality was successfully validated in several *in vitro* and *in vivo* model systems across different cancer cell types, and without wishing to be bound by theory it was postulated that targeting SMARCA2 could represent a promising approach to tackle SMARCA4-mutated cancers.

SMARCA2 and SMARCA4 are multidomain proteins containing protein:protein interaction domains, ATPase domain and a bromodomain known to bind to acetylated lysines on histone H3 and H4 tails. Recent complementary cDNA rescue experiments and pharmacological studies with selective bromodomain inhibitors revealed that the dependency on SMARCA2 can be attributed to an intact ATPase function of SMARCA2, but not to its other domain functions. SMARCA2 is not an essential gene, and its inactivation results in viable animals without any overt deficiencies (Reyes JC et al., 1998, EMBO J); therefore, pharmacological inhibition of the ATPase function of this enzyme may provide an attractive novel therapeutic opportunity to treat SMARCA4 mutation-driven cancers.

Various urea compounds are known for crop protection. From J. Med. Chem., DOI: 10.1021/acs.jmedchem.8b01318 • Publication Date (Web): 19 Oct 2018 some urea compounds are known.

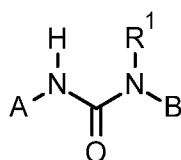
SUMMARY

The invention generally provides urea compounds of general formula (I) of the present invention as described and defined herein.

As reported in detail below, it has now been found, and this partially constitutes the basis of the present invention, that the compounds of the present invention do have antiproliferative activity.

In particular, the compounds of the present invention have surprisingly been found to
5 inhibit SMARCA2 for which data are given in the biological experimental section and such compounds may therefore be used for the treatment or prophylaxis of hyperproliferative disorders, such as cancer disorders, for example.

In accordance with a first aspect, the present invention covers compounds of general
10 formula (I):



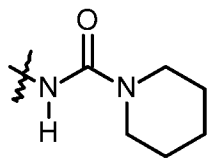
(I),

in which

- A is a pyridinyl group which is optionally substituted by R² and/or R³;
- 15 R¹ is a hydrogen atom or a methyl group;
- R² is a halogen atom;
- R³ is a hydrogen atom, a halogen atom or a C₁-C₃-alkyl group;
- B a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from
- 20 a halogen atom,
a C₁-C₃-alkyl group,
a C₁-C₃-haloalkyl group,
a C₁-C₃-alkoxy group,
a cyano group,
- 25 a hydroxy group,
a SF₅ group,
a -S(O)₂-(C₁-C₃-alkyl) group,
a N(O)₂ group,
a heteroaryl group,
- 30 a heterocycloalkyl group,

a $-O-(C_1-C_3\text{-alkyl})\text{-heterocycloalkyl}$,

a $-S(O)_2\text{-heterocycloalkyl}$ group,



a group and

a $C(O)NR^4R^5$, wherein

5 R^4 is a hydrogen atom or a $C_1-C_3\text{-alkyl}$ group;

R^5 is a hydrogen atom, a $C_1-C_3\text{-alkyl}$ group, or a heteroaryl group;

a pyridinyl group,

which is optionally substituted with one or more substituents and each substituent is independently selected from

10 a halogen atom,

a cyano group,

a $C_1-C_3\text{-alkyl}$ group,

a $C_1-C_3\text{-haloalkyl}$ group,

a $C_1-C_3\text{-alkoxy}$ group,

15 a $C_3-C_6\text{-cycloalkyl}$ group,

a phenyl group, which is optionally substituted with a halogen atom, a C_1 -

$C_3\text{-alkyl}$ group, $C_1-C_3\text{-alkoxy}$ group, a CN group, a NR^4R^5 group;

a heteroaryl group and

a piperazinyl group, which is optionally substituted with a $C(O)R^6$ group,

20 wherein

R^6 is a $C_1-C_4\text{-alkyl}$ group;

a pyrimidinyl group,

which is optionally substituted with a $C_1-C_3\text{-alkyl}$ group, or

a piperazinyl group,

25 which is optionally further substituted with a $C_1-C_3\text{-alkyl}$ group;

a thiazolyl group, which is optionally substituted one or two times and each substituent is independently selected from

a $C_1-C_4\text{-alkyl}$ group,

a phenyl group which itself is optionally further substituted with a halogen

30 atom or a $C_1-C_3\text{-haloalkyl}$ group, and

- a -CH₂-phenyl group which itself is optionally further substituted with a cyano group;
- a pyrazolyl group, which is optionally substituted one or more times with a C₁-C₄-alkyl group or a phenyl group which itself is optionally substituted with a halogen atom,
- a thiadiazolyl group which is optionally substituted with a phenyl group which itself is optionally substituted with a C₁-C₃-haloalkyl group, or a phenyl group which itself is optionally substituted with a halogen atom or a C₁-C₃-haloalkyl group;
- a benzofuranyl group, which is optionally substituted with a C(O)NR⁴R⁵ group,
- a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen atom;
- an indazolyl group which is optionally substituted one or more substituents and each substituent independently selected from a halogen atom, a C₁-C₃-alkyl group, a C₁-C₃-haloalkyl group,
- an isoquinolinyl group which is optionally substituted with a halogen atom, and an dihydroindenyl group;
- with the proviso that
- 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
- 1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
- 1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
- 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
- 1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
- 1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded,
- or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

DETAILED DESCRIPTION

DEFINITIONS

- The term “substituted” means that one or more hydrogen atoms on the designated atom or group are replaced with a selection from the indicated group, provided that the designated atom's normal valency under the existing circumstances is not exceeded. Combinations of substituents and/or variables are permissible.

The term "optionally substituted" means that the number of substituents can be equal to or different from zero. Unless otherwise indicated, it is possible that optionally substituted groups are substituted with as many optional substituents as can be accommodated by replacing a hydrogen atom with a non-hydrogen substituent on any available carbon or nitrogen atom. Commonly, it is possible for the number of optional substituents, when present, to be 1, 2, or 3, in particular 1, or 2.

When groups in the compounds according to the invention are substituted, it is possible for said groups to be mono-substituted or poly-substituted with substituent(s), unless otherwise specified. Within the scope of the present invention, the meanings of all groups which occur repeatedly are independent from one another. It is possible that groups in the compounds according to the invention are substituted with one, two or three identical or different substituents, particularly with one substituent.

The term "ring substituent" means a substituent attached to an aromatic or nonaromatic ring which replaces an available hydrogen atom on the ring.

The term "comprising" when used in the specification includes "consisting of".

If within the present text any item is referred to as "as mentioned herein", it means that it may be mentioned anywhere in the present text.

The terms as mentioned in the present text have the following meanings:

The term "halogen atom" means a fluorine, chlorine, or bromine atom, particularly a fluorine or chlorine atom.

The term "C₁-C₄-alkyl" means a linear or branched, saturated, monovalent hydrocarbon group having 1, 2, 3, or 4 carbon atoms, e.g. a methyl-, ethyl-, propyl-, *iso*-propyl-, *n*-butyl-, *iso*-butyl-, *sec*-butyl-, and a *tert*-butyl group, or an isomer thereof. Particularly, said group has 1, 2, or 3 carbon atoms ("C₁-C₃-alkyl"), e.g. a methyl-, ethyl-, propyl-, and an isopropyl group.

The term "C₁-C₃-haloalkyl" means a linear or branched, saturated, monovalent hydrocarbon group in which the term "C₁-C₃-alkyl" is as defined *supra*, and in which one or more of the hydrogen atoms are replaced, identically or differently, with a halogen atom. Particularly, said halogen atom is a fluorine atom. Said C₁-C₃-haloalkyl group is, for example, a fluoromethyl-, difluoromethyl-, trifluoromethyl-, 2-fluoroethyl-, 2,2-difluoroethyl-, 2,2,2-trifluoroethyl-, pentafluoroethyl-, 3,3,3-trifluoropropyl- and a 1,3-difluoropropan-2-yl group.

The term "C₁-C₆-alkoxy" means a linear or branched, saturated, monovalent group of formula (C₁-C₆-alkyl)-O-, in which the term "C₁-C₆-alkyl" group is as defined *supra*, e.g. a

methoxy-, ethoxy-, *n*-propoxy-, isopropoxy-, *n*-butoxy-, *sec*-butoxy-, isobutoxy-, *tert*-butoxy-, pentyloxy-, isopentyloxy- or a *n*-hexyloxy group, or an isomer thereof.

The term "C₃-C₆-cycloalkyl" means a saturated, monovalent, mono- or bicyclic hydrocarbon ring which contains 3, 4, 5, or 6, carbon atoms ("C₃-C₆-cycloalkyl"). Said C₃-C₆-cycloalkyl group is for example, a monocyclic hydrocarbon ring, e.g. a cyclopropyl-, cyclobutyl-, cyclopentyl- and a cyclohexyl group.

The term "heterocycloalkyl" refers to the terms "4- to 7-membered heterocycloalkyl" and "4- to 6-membered heterocycloalkyl" which means a monocyclic, saturated heterocycle with 4, 5, 6 or 7 or, respectively, 4, 5 or 6 ring atoms in total, which contains one or two identical or different ring heteroatoms from the series N, O and S, it being possible for said heterocycloalkyl group to be attached to the rest of the molecule via any one of the carbon atoms or, if present, a nitrogen atom.

Said heterocycloalkyl group, without being limited thereto, can be a 4-membered ring, such as azetidiny-, oxetanyl or thietanyl, for example; or a 5-membered ring, such as a tetrahydrofuranyl-, 1,3-dioxolanyl-, thiolanyl-, pyrrolidinyl-, imidazolidinyl-, pyrazolidinyl-, 1,1-dioxidothiolanyl-, 1,2-oxazolidinyl-, 1,3-oxazolidinyl- and a 1,3-thiazolidinyl group, for example; or a 6-membered ring, such as a tetrahydropyranyl-, tetrahydrothiopyranyl-, piperidinyl-, morpholinyl-, dithianyl-, thiomorpholinyl-, piperazinyl-, 1,3-dioxanyl-, 1,4-dioxanyl- and a 1,2-oxazinanyl group, for example, or a 7-membered ring, such as an azepanyl-, 1,4-diazepanyl- and a 1,4-oxazepanyl group, for example.

The term "heteroaryl" means a monovalent, monocyclic or bicyclic aromatic ring having 5, 6, 8, 9 or 10 ring atoms (a "5- to 10-membered heteroaryl" group), particularly 6 to 10 ring atoms, which contains at least one ring heteroatom and optionally one further ring heteroatom from the series: N, O and/or S, and which is bound via a ring carbon atom or optionally via a ring nitrogen atom (if allowed by valency).

Said heteroaryl group can be a 5-membered heteroaryl group, such as, for example a thienyl-, furanyl-, pyrrolyl-, oxazolyl-, thiazolyl-, imidazolyl-, pyrazolyl-, isoxazolyl-, isothiazolyl-, oxadiazolyl-, oxadiazolonyl-, triazolyl-, thiadiazolyl- or a tetrazolyl group; or a 6-membered heteroaryl group, such as, for example, a pyridyl-, pyridazinyl-, pyrimidinyl-, pyrazinyl- or a triazinyl group; or a 9- to 10-membered heteroaryl group, such as, for example, a benzofuranyl-, benzothienyl-, benzoxazolyl-, benzisoxazolyl-, benzimidazolyl-, benzothiazolyl-, benzotriazolyl-, indazolyl-, indolyl-, isoindolyl-, indoliziny-, purinyl-, quinolyl-, and an isoquinolyl group;.

In general, and unless otherwise mentioned, the heteroaryl or heteroarylene groups include all possible isomeric forms thereof, e.g.: tautomers and positional isomers with

respect to the point of linkage to the rest of the molecule. Thus, for some illustrative non-restricting examples, the term pyridinyl includes pyridin-2-yl, pyridin-3-yl and pyridin-4-yl; or the term thienyl includes thien-2-yl and thien-3-yl.

Particularly, the pyridinyl group is a pyridin-2-yl-, pyridin-3-yl- or a pyridin-4-yl group, more particularly the pyridinyl group A is a pyridin-4-yl group.

The term "C₁-C₄", as used in the present text, *e.g.* in the context of the definition of "C₁-C₄-alkyl", "C₁-C₄-haloalkyl", "C₁-C₄-hydroxyalkyl", "C₁-C₄-alkoxy" or "C₁-C₄-haloalkoxy" means an alkyl group having a finite number of carbon atoms of 1 to 6, *i.e.* 1, 2, 3 or 4 carbon atoms.

Further, as used herein, the term "C₃-C₆", as used in the present text, *e.g.* in the context of the definition of "C₃-C₆-cycloalkyl", means a cycloalkyl group having a finite number of carbon atoms of 3 to 6, *i.e.* 3, 4, 5, or 6 carbon atoms.

When a range of values is given, said range encompasses each value and sub-range within said range, for example:

"C₁-C₆" encompasses C₁, C₂, C₃, C₄, C₅, C₆, C₁-C₆, C₁-C₅, C₁-C₄, C₁-C₃, C₁-C₂, C₂-C₆, C₂-C₅, C₂-C₄, C₂-C₃, C₃-C₆, C₃-C₅, C₃-C₄, C₄-C₆, C₄-C₅, and C₅-C₆;

"C₃-C₁₀" encompasses C₃, C₄, C₅, C₆, C₇, C₈, C₉, C₁₀, C₃-C₁₀, C₃-C₉, C₃-C₈, C₃-C₇, C₃-C₆, C₃-C₅, C₃-C₄, C₄-C₁₀, C₄-C₉, C₄-C₈, C₄-C₇, C₄-C₆, C₄-C₅, C₅-C₁₀, C₅-C₉, C₅-C₈, C₅-C₇, C₅-C₆, C₆-C₁₀, C₆-C₉, C₆-C₈, C₆-C₇, C₇-C₁₀, C₇-C₉, C₇-C₈, C₈-C₁₀, C₈-C₉ and C₉-C₁₀;

"C₃-C₈" encompasses C₃, C₄, C₅, C₆, C₇, C₈, C₃-C₈, C₃-C₇, C₃-C₆, C₃-C₅, C₃-C₄, C₄-C₈, C₄-C₇, C₄-C₆, C₄-C₅, C₅-C₈, C₅-C₇, C₅-C₆, C₆-C₈, C₆-C₇ and C₇-C₈;

"C₃-C₆" encompasses C₃, C₄, C₅, C₆, C₃-C₆, C₃-C₅, C₃-C₄, C₄-C₆, C₄-C₅, and C₅-C₆;

As used herein, the term "leaving group" refers to an atom or a group of atoms that is displaced in a chemical reaction as stable species taking with it the bonding electrons, *e.g.*, typically forming an anion. For example, a leaving group may be selected from the group comprising: halo, in particular a chloro, bromo or iodo, (methylsulfonyl)oxy-, [(4-methylphenyl)sulfonyl]oxy-, [(trifluoromethyl)sulfonyl]oxy-, [(nonafluorobutyl)sulfonyl]oxy-, [(4-bromophenyl)sulfonyl]oxy-, [(4-nitrophenyl)sulfonyl]oxy-, [(2-nitrophenyl)sulfonyl]oxy-, [(4-isopropylphenyl)sulfonyl]oxy-, [(2,4,6-triisopropylphenyl)sulfonyl]oxy-, [(2,4,6-trimethylphenyl)sulfonyl]oxy-, [(4-*tert*-butylphenyl)sulfonyl]oxy-, (phenylsulfonyl)oxy- and a [(4-methoxyphenyl)sulfonyl]oxy group.

It is possible for the compounds of general formula (I) to exist as isotopic variants. The invention therefore includes one or more isotopic variant(s) of the compounds of general formula (I), particularly deuterium-containing compounds of general formula (I).

5 The term "Isotopic variant" of a compound or a reagent is defined as a compound exhibiting an unnatural proportion of one or more of the isotopes that constitute such a compound.

The term "Isotopic variant of the compound of general formula (I)" is defined as a compound of general formula (I) exhibiting an unnatural proportion of one or more of the isotopes that constitute such a compound.

10 The expression "unnatural proportion" means a proportion of such isotope which is higher than its natural abundance. The natural abundances of isotopes to be applied in this context are described in "Isotopic Compositions of the Elements 1997", Pure Appl. Chem., 70(1), 217-235, 1998.

15 Examples of such isotopes include stable and radioactive isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, sulfur, fluorine, chlorine, bromine and iodine, such as ^2H (deuterium), ^3H (tritium), ^{11}C , ^{13}C , ^{14}C , ^{15}N , ^{17}O , ^{18}O , ^{32}P , ^{33}P , ^{33}S , ^{34}S , ^{35}S , ^{36}S , ^{18}F , ^{36}Cl , ^{82}Br , ^{123}I , ^{124}I , ^{125}I , ^{129}I and ^{131}I , respectively.

20 With respect to the treatment and/or prophylaxis of the disorders specified herein the isotopic variant(s) of the compounds of general formula (I) may contain deuterium ("deuterium-containing compounds of general formula (I)"). Isotopic variants of the compounds of general formula (I) in which one or more radioactive isotopes, such as ^3H or ^{14}C , are incorporated are useful e.g. in drug and/or substrate tissue distribution studies. Positron emitting isotopes such as ^{18}F or ^{11}C may be incorporated into a compound of general formula (I). These isotopic variants of the compounds of general formula (I) are
25 useful for in vivo imaging applications. Deuterium-containing and ^{13}C -containing compounds of general formula (I) can be used in mass spectrometry analyses in the context of preclinical or clinical studies.

Isotopic variants of the compounds of general formula (I) can generally be prepared by methods known to a person skilled in the art, such as those described in the schemes
30 and/or examples herein, by substituting a reagent for an isotopic variant of said reagent, such as a deuterium-containing reagent. Depending on the desired sites of deuteration, in some cases deuterium from D_2O can be incorporated either directly into the compounds or into reagents that are useful for synthesizing such compounds. Deuterium gas is also a useful reagent for incorporating deuterium into molecules. Catalytic
35 deuteration of olefinic bonds and acetylenic bonds is a rapid route for incorporation of

deuterium. Metal catalysts (i.e. Pd, Pt, and Rh) in the presence of deuterium gas can be used to directly exchange deuterium for hydrogen in functional groups containing hydrocarbons. A variety of deuterated reagents and synthetic building blocks are commercially available from companies such as for example C/D/N Isotopes, Quebec, Canada; Cambridge Isotope Laboratories Inc., Andover, MA, USA; and CombiPhos Catalysts, Inc., Princeton, NJ, USA.

The term "deuterium-containing compound of general formula (I)" is defined as a compound of general formula (I), in which one or more hydrogen atom(s) is/are replaced by one or more deuterium atom(s) and in which the abundance of deuterium at each deuterated position of the compound of general formula (I) is higher than the natural abundance of deuterium, which is about 0.015%. Particularly, in a deuterium-containing compound of general formula (I) the abundance of deuterium at each deuterated position of the compound of general formula (I) is higher than 10%, 20%, 30%, 40%, 50%, 60%, 70% or 80%, higher than 90%, 95%, 96% or 97%, even higher than 98% or 99% at said position(s). It is understood that the abundance of deuterium at each deuterated position is independent of the abundance of deuterium at other deuterated position(s).

The selective incorporation of one or more deuterium atom(s) into a compound of general formula (I) may alter the physicochemical properties (such as for example acidity [C. L. Perrin, et al., J. Am. Chem. Soc., 2007, 129, 4490], basicity [C. L. Perrin et al., J. Am. Chem. Soc., 2005, 127, 9641], lipophilicity [B. Testa et al., Int. J. Pharm., 1984, 19(3), 271]) and/or the metabolic profile of the molecule and may result in changes in the ratio of parent compound to metabolites or in the amounts of metabolites formed. Such changes may result in certain therapeutic advantages and hence may be preferred in some circumstances. Reduced rates of metabolism and metabolic switching, where the ratio of metabolites is changed, have been reported (A. E. Mutlib et al., Toxicol. Appl. Pharmacol., 2000, 169, 102). These changes in the exposure to parent drug and metabolites can have important consequences with respect to the pharmacodynamics, tolerability and efficacy of a deuterium-containing compound of general formula (I). In some cases deuterium substitution reduces or eliminates the formation of an undesired or toxic metabolite and enhances the formation of a desired metabolite (e.g. Nevirapine: A. M. Sharma et al., Chem. Res. Toxicol., 2013, 26, 410; Efavirenz: A. E. Mutlib et al., Toxicol. Appl. Pharmacol., 2000, 169, 102). In other cases the major effect of deuteration is to reduce the rate of systemic clearance. As a result, the biological half-life of the compound is increased. The potential clinical benefits would include the ability to maintain similar systemic exposure with decreased peak levels and increased trough levels. This could result in lower side effects and enhanced efficacy, depending on the particular

compound's pharmacokinetic/ pharmacodynamic relationship. ML-337 (C. J. Wenthur et al., J. Med. Chem., 2013, 56, 5208) and Odanacatib (K. Kassahun et al., WO2012/112363) are examples for this deuterium effect. Still other cases have been reported in which reduced rates of metabolism result in an increase in exposure of the drug without changing the rate of systemic clearance (e.g. Rofecoxib: F. Schneider et al., 5 Arzneim. Forsch. / Drug. Res., 2006, 56, 295; Telaprevir: F. Maltais et al., J. Med. Chem., 2009, 52, 7993). Deuterated drugs showing this effect may have reduced dosing requirements (e.g. lower number of doses or lower dosage to achieve the desired effect) and/or may produce lower metabolite loads.

10 A compound of general formula (I) may have multiple potential sites of attack for metabolism. To optimize the above-described effects on physicochemical properties and metabolic profile, deuterium-containing compounds of general formula (I) having a certain pattern of one or more deuterium-hydrogen exchange(s) can be selected. Particularly, the deuterium atom(s) of deuterium-containing compound(s) of general formula (I) is/are 15 attached to a carbon atom and/or is/are located at those positions of the compound of general formula (I), which are sites of attack for metabolizing enzymes such as e.g. cytochrome P₄₅₀.

In another embodiment the present invention concerns a deuterium-containing compound of general formula (I), comprising one or more groups selected from -CD₃, - 20 OCD₃, benzylic CD₂, and N-D.

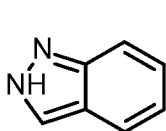
Where the plural form of the word compounds, salts, polymorphs, hydrates, solvates and the like, is used herein, this is taken to mean also a single compound, salt, polymorph, isomer, hydrate, solvate or the like.

By "stable compound" or "stable structure" is meant a compound that is sufficiently robust 25 to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

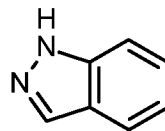
The present invention includes all possible stereoisomers of the compounds of the present invention as single stereoisomers, or as any mixture of said stereoisomers, e.g. (R)- or (S)- isomers, cis-/trans isomers, E-/Z-isomers in any ratio. Isolation of a single 30 stereoisomer, e.g. a single enantiomer or a single diastereomer, of a compound of the present invention is achieved by any suitable state of the art method, such as chromatography, especially chiral chromatography, for example.

Further, it is possible for the compounds of the present invention to exist as tautomers. For example, any compound of the present invention which contains an imidazopyridine

moiety as a heteroaryl group for example can exist as a 1H tautomer, or a 3H tautomer, or even a mixture in any amount of the two tautomers, namely :



2H tautomer



1H tautomer

The present invention includes all possible tautomers of the compounds of the present invention as single tautomers, or as any mixture of said tautomers, in any ratio.

Further, the compounds of the present invention can exist as N-oxides, which are defined in that at least one nitrogen of the compounds of the present invention is oxidised. The present invention includes all such possible N-oxides.

The present invention also covers useful forms of the compounds of the present invention, such as metabolites, hydrates, solvates, prodrugs, salts, in particular pharmaceutically acceptable salts, and/or co-precipitates.

The compounds of the present invention can exist as a hydrate, or as a solvate, wherein the compounds of the present invention contain polar solvents, in particular water, methanol or ethanol for example, as structural element of the crystal lattice of the compounds. It is possible for the amount of polar solvents, in particular water, to exist in a stoichiometric or non-stoichiometric ratio. In the case of stoichiometric solvates, *e.g.* a hydrate, hemi-, (semi-), mono-, sesqui-, di-, tri-, tetra-, penta- *etc.* solvates or hydrates, respectively, are possible. The present invention includes all such hydrates or solvates.

Further, it is possible for the compounds of the present invention to exist in free form, *e.g.* as a free base, or as a free acid, or as a zwitterion, or to exist in the form of a salt. Said salt may be any salt, either an organic or inorganic addition salt, particularly any pharmaceutically acceptable organic or inorganic addition salt, which is customarily used in pharmacy, or which is used, for example, for isolating or purifying the compounds of the present invention.

The term "pharmaceutically acceptable salt" refers to an inorganic or organic acid addition salt of a compound of the present invention. For example, see S. M. Berge, *et al.* "Pharmaceutical Salts," J. Pharm. Sci. 1977, 66, 1-19.

A suitable pharmaceutically acceptable salt of the compounds of the present invention may be, for example, an acid-addition salt of a compound of the present invention bearing a nitrogen atom, in a chain or in a ring, for example, which is sufficiently basic, such as

an acid-addition salt with an inorganic acid, or "mineral acid", such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, bisulfuric acid, phosphoric acid, and nitric acid or with an organic acid, such as formic acid, acetic acid, acetoacetic acid, pyruvic acid, trifluoroacetic acid, propionic acid, butyric acid, hexanoic acid, heptanoic acid, undecanoic acid, lauric acid, benzoic acid, salicylic acid, 2-(4-hydroxybenzoyl)-benzoic acid, camphoric acid, cinnamic acid, cyclopentanepropionic acid, digluconic acid, 3-hydroxy-2-naphthoic acid, nicotinic acid, pamoic acid, pectinic acid, persulfuric acid, 3-phenylpropionic acid, picric acid, pivalic acid, 2-hydroxyethanesulfonate acid, itaconic acid, sulfamic acid, trifluoromethanesulfonic acid, dodecylsulfuric acid, ethansulfonic acid, benzenesulfonic acid, para-toluenesulfonic acid, methansulfonic acid, 2-naphthalenesulfonic acid, naphthalenedisulfonic acid, camphorsulfonic acid, citric acid, tartaric acid, stearic acid, lactic acid, oxalic acid, malonic acid, succinic acid, malic acid, adipic acid, alginic acid, maleic acid, fumaric acid, D-gluconic acid, mandelic acid, ascorbic acid, glucoheptanoic acid, glycerophosphoric acid, aspartic acid, sulfosalicylic acid, hemisulfuric acid and thiocyanic acid, for example.

Further, another suitably pharmaceutically acceptable salt of a compound of the present invention which is sufficiently acidic, is an alkali metal salt, for example a sodium or potassium salt, an alkaline earth metal salt, for example a calcium, magnesium or strontium salt, or an aluminium or a zinc salt, or an ammonium salt derived from ammonia or from an organic primary, secondary or tertiary amine having 1 to 20 carbon atoms, such as ethylamine, diethylamine, triethylamine, ethyldiisopropylamine, monoethanolamine, diethanolamine, triethanolamine, dicyclohexylamine, dimethylaminoethanol, diethylaminoethanol, tris(hydroxymethyl)aminomethane, procaine, dibenzylamine, *N*-methylmorpholine, arginine, lysine, 1,2-ethylenediamine, *N*-methylpiperidine, *N*-methyl-glucamine, *N,N*-dimethyl-glucamine, *N*-ethyl-glucamine, 1,6-hexanediamine, glucosamine, sarcosine, serinol, 2-amino-1,3-propanediol, 3-amino-1,2-propanediol, 4-amino-1,2,3-butanetriol, or a salt with a quaternary ammonium ion having 1 to 20 carbon atoms, such as tetramethylammonium, tetraethylammonium, tetra(*n*-propyl)ammonium, tetra(*n*-butyl)ammonium, *N*-benzyl-*N,N,N*-trimethylammonium, choline or benzalkonium.

Those skilled in the art will further recognise that it is possible for acid addition salts of the claimed compounds to be prepared by reaction of the compounds with the appropriate inorganic or organic acid via any of a number of known methods. Alternatively, alkali and alkaline earth metal salts of acidic compounds of the present invention are prepared by reacting the compounds of the present invention with the appropriate base via a variety of known methods.

The present invention includes all possible salts of the compounds of the present invention as single salts, or as any mixture of said salts, in any ratio.

In the present text, in particular in the Experimental Section, for the synthesis of intermediates and of examples of the present invention, when a compound is mentioned
5 as a salt form with the corresponding base or acid, the exact stoichiometric composition of said salt form, as obtained by the respective preparation and/or purification process, is, in most cases, unknown.

Unless specified otherwise, suffixes to chemical names or structural formulae relating to salts, such as "hydrochloride", "trifluoroacetate", "sodium salt", or "x HCl", "x CF₃COOH",
10 "x Na⁺", for example, mean a salt form, the stoichiometry of which salt form not being specified.

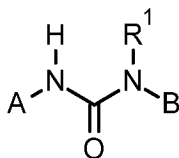
This applies analogously to cases in which synthesis intermediates or example compounds or salts thereof have been obtained, by the preparation and/or purification processes described, as solvates, such as hydrates, with (if defined) unknown
15 stoichiometric composition.

Furthermore, the present invention includes all possible crystalline forms, or polymorphs, of the compounds of the present invention, either as single polymorph, or as a mixture of more than one polymorph, in any ratio.

Moreover, the present invention also includes prodrugs of the compounds according to
20 the invention. The term "prodrugs" here designates compounds which themselves can be biologically active or inactive, but are converted (for example metabolically or hydrolytically) into compounds according to the invention during their residence time in the body.

DESCRIPTION

25 In accordance with a first aspect, the present invention covers compounds of general formula (I):



(I),

in which

A is a pyridinyl group which is optionally substituted by R^2 and/or R^3 ;

R^1 is a hydrogen atom or a methyl group;

R^2 is a halogen atom;

R^3 is a hydrogen atom, a halogen atom or a C_1 - C_3 -alkyl group;

5 B a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom,

a C_1 - C_3 -alkyl group,

a C_1 - C_3 -haloalkyl group,

10 a C_1 - C_3 -alkoxy group,

a cyano group,

a hydroxy group,

a SF_5 group,

a $-S(O)_2$ -(C_1 - C_3 -alkyl) group,

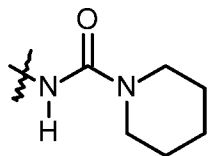
15 a $N(O)_2$ group,

a heteroaryl group,

a heterocycloalkyl group,

a $-O$ -(C_1 - C_3 -alkyl)-heterocycloalkyl,

a $-S(O)_2$ -heterocycloalkyl group,



20 a group and

a $C(O)NR^4R^5$, wherein

R^4 is a hydrogen atom or a C_1 - C_3 -alkyl group;

R^5 is a hydrogen atom, a C_1 - C_3 -alkyl group, or a heteroaryl group;

a pyridinyl group,

25 which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom,

a cyano group,

a C_1 - C_3 -alkyl group,

30 a C_1 - C_3 -haloalkyl group,

a C_1 - C_3 -alkoxy group,

a C_3 - C_6 -cycloalkyl group,

a phenyl group, which is optionally substituted with a halogen atom, a C₁-C₃-alkyl group, C₁-C₃-alkoxy group, a CN group, a NR⁴R⁵ group; a heteroaryl group and

a piperazinyl group, which is optionally substituted with a C(O)R⁶ group, wherein

R⁶ is a C₁-C₄-alkyl group;

a pyrimidinyl group,

which is optionally substituted with a C₁-C₃-alkyl group, or

a piperazinyl group,

which is optionally further substituted with a C₁-C₃-alkyl group;

a thiazolyl group, which is optionally substituted one or two times and each substituent is independently selected from

a C₁-C₄-alkyl group,

a phenyl group which itself is optionally further substituted with a halogen atom or a C₁-C₃-haloalkyl group, and

a -CH₂-phenyl group which itself is optionally further substituted with a cyano group;

a pyrazolyl group, which is optionally substituted one or more times with a C₁-C₄-alkyl group or a phenyl group which itself is optionally substituted with a halogen atom,

a thiadiazolyl group which is optionally substituted with a phenyl group which itself is optionally substituted with a C₁-C₃-haloalkyl group, or a phenyl group which itself is optionally substituted with a halogen atom or a C₁-C₃-haloalkyl group;

a benzofuranyl group, which is optionally substituted with a C(O)NR⁴R⁵ group,

a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen atom;

an indazolyl group which is optionally substituted one or more substituents and each substituent independently selected from a halogen atom, a C₁-C₃-alkyl group, a C₁-C₃-haloalkyl group,

an isoquinolinyl group which is optionally substituted with a halogen atom, and an dihydroindenyl group;

with the proviso that

1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,

1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,

5 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,

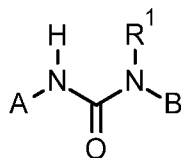
1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and

1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded,

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a

10 mixture of same.

In accordance with another aspect, the present invention covers compounds of general formula (I):



15

(I),

in which

A is a pyridinyl group which is optionally substituted by R² and/or R³;

R¹ is a hydrogen atom or a methyl group;

R² is a halogen atom;

20 R³ is a hydrogen atom, a halogen atom or a C₁-C₃-alkyl group;

B a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom,

a C₁-C₃-alkyl group,

25 a C₁-C₃-haloalkyl group,

a C₁-C₃-alkoxy group,

a cyano group,

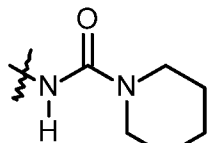
a hydroxy group,

a SF₅ group,

30 a -S(O)₂-(C₁-C₃-alkyl) group,

a $N(O)_2$ group,
a heteroaryl group,
a heterocycloalkyl group,
a $-O-(C_1-C_3\text{-alkyl})\text{-heterocycloalkyl}$,
a $-S(O)_2\text{-heterocycloalkyl}$ group,

5



a group and
a $C(O)NR^4R^5$, wherein

R^4 is a hydrogen atom or a $C_1-C_3\text{-alkyl}$ group;

R^5 is a hydrogen atom, a $C_1-C_3\text{-alkyl}$ group, or a heteroaryl group;

10

a pyridinyl group,

which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom,

a cyano group,

15

a $C_1-C_3\text{-alkyl}$ group,

a $C_1-C_3\text{-haloalkyl}$ group,

a $C_1-C_3\text{-alkoxy}$ group,

a $C_3-C_6\text{-cycloalkyl}$ group,

a phenyl group, which is optionally substituted with a halogen atom, a $C_1\text{-}$

20

$C_3\text{-alkyl}$ group, $C_1-C_3\text{-alkoxy}$ group, a CN group, a NR^4R^5 group;

a heteroaryl group and

a piperazinyl group, which is optionally substituted with a $C(O)R^6$ group,
wherein

R^6 is a $C_1-C_4\text{-alkyl}$ group;

25

a pyrimidinyl group,

which is optionally substituted with a $C_1-C_3\text{-alkyl}$ group, or

a piperazinyl group,

which is optionally further substituted with a $C_1-C_3\text{-alkyl}$ group;

a thiazolyl group, which is optionally substituted one or two times and each substituent is independently selected from

30

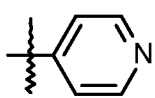
a $C_1-C_4\text{-alkyl}$ group,

- a phenyl group which itself is optionally further substituted with a halogen atom or a C₁-C₃-haloalkyl group, and
- a -CH₂-phenyl group which itself is optionally further substituted with a cyano group;
- 5 a pyrazolyl group, which is optionally substituted one or more times with a C₁-C₄-alkyl group or a phenyl group which itself is optionally substituted with a halogen atom,
- a thiadiazolyl group which is optionally substituted with a phenyl group which itself is optionally substituted with a C₁-C₃-haloalkyl group, or a phenyl group which
- 10 itself is optionally substituted with a halogen atom or a C₁-C₃-haloalkyl group;
- a benzofuranyl group, which is optionally substituted with a C(O)NR⁴R⁵ group,
- a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen atom;
- an indazolyl group which is optionally substituted one or more substituents and
- 15 each substituent independently selected from a halogen atom, a C₁-C₃-alkyl group, a C₁-C₃-haloalkyl group,
- an isoquinolinyl group which is optionally substituted with a halogen atom, and
- an dihydroindenyl group;
- with the proviso that the following compounds are excluded
- 20 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-methyl-1H-imidazol-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
- 25 1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3-methylisothiazol-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3-(trifluoromethyl)isothiazol-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3-(difluoromethyl)isothiazol-5-yl)urea
- 30 1-(5-amino-2-chloropyridin-4-yl)-3-(3-(difluoromethyl)isothiazol-5-yl)urea,
1-(2-chloro-5-(hydroxymethyl)pyridin-4-yl)-3-(3-(difluoromethyl)isothiazol-5-yl)urea,
1-(5-amino-2-fluoropyridin-4-yl)-3-(3-(difluoromethyl)isothiazol-5-yl)urea,
1-(3-(difluoromethyl)isothiazol-5-yl)-3-(2-fluoro-5-(hydroxymethyl)pyridin-4-yl)urea,

3-((4-(3-(2-chloropyridin-4-yl)ureido)pyridin-2-yl)ethynyl)benzoic acid, and
 1-(5-amino-2-chloropyridin-4-yl)-3-(4-bromo-3-((3-(hydroxymethyl)phenyl)ethynyl)
 isothiazol-5-yl)urea;

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a
 5 stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a
 mixture of same.

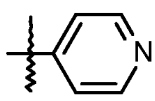
In accordance with a second embodiment of the first aspect, the present invention covers
 compounds of general formula (I), *supra*, in which:

- A is a  group which is optionally substituted by R² and/or R³;
- 10 R¹ is a hydrogen atom;
- R² is a halogen atom;
- R³ is a hydrogen atom or a halogen atom;
- B is a phenyl group, which is optionally substituted with one or more substituents
 and each substituent is independently selected from
- 15 a halogen atom,
 a C₁-C₃-alkyl group,
 a C₁-C₃-haloalkyl group,
 a C₁-C₃-alkoxy group,
 a cyano group,
- 20 a hydroxy group,
 a heteroaryl group,
 a heterocycloalkyl group,
 a C(O)NR⁴R⁵, wherein
- R⁴ is a hydrogen atom or a C₁-C₃-alkyl group;
- 25 R⁵ is a hydrogen atom, a C₁-C₃-alkyl group, a heteroaryl group or
 a -(C₁-C₃-alkyl)-O-heteroaryl group;
- a pyridinyl group,
 which is optionally substituted with one or more substituents and each
 substituent is independently selected from
- 30 a halogen atom,
 a cyano group,

- a C₁-C₃-alkyl group,
a C₁-C₃-haloalkyl group,
a C₁-C₃-alkoxy group,
a phenyl group, a heteroaryl group, and
5 a piperazinyl group, which is optionally substituted with a C(O)R⁶ group,
wherein
R⁶ is a C₁-C₄-alkyl group,
a pyrimidinyl group which is optionally substituted with a C₁-C₃-alkyl group, or a
piperazinyl group which itself is optionally further substituted with a C₁-C₃-
10 alkyl group;
a thiazol-2-yl group, which is optionally substituted one or two times and each
substituent is independently selected from
a C₁-C₄-alkyl group,
a phenyl group which itself is optionally further substituted with a halogen
15 atom or a C₁-C₃-haloalkyl group, and
a -CH₂-phenyl group which itself is optionally further substituted with a
cyano group;
a pyrazol-5-yl group, which is optionally substituted one or more times with a C₁-
C₄-alkyl group or a phenyl group which itself is optionally substituted with
20 a halogen atom;
a benzofuran-3-yl group, which is optionally substituted with a C(O)NR⁴R⁵ group;
a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen
atom; and
an indazol-7-yl group which is optionally substituted one or more substituents and
25 each substituent independently selected from a halogen atom, a C₁-C₃-
alkyl group, a C₁-C₃-haloalkyl group;
with the proviso that
1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
30 1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In accordance with a third embodiment of the first aspect, the present invention covers
 5 compounds of general formula (I), *supra*, in which:

A is a  group which is optionally substituted by R² and/or R³;

R¹ is a hydrogen atom;

R² is a halogen atom;

R³ is a hydrogen atom;

10 B is a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom,

a C₁-C₃-alkyl group,

a C₁-C₃-haloalkyl group, and

15 a C₁-C₃-alkoxy group,

a cyano group,

a heteroaryl group

a pyridinyl group,

which is optionally substituted with one or more substituents and each

20 substituent is independently selected from

a halogen atom,

a cyano group

a C₁-C₃-alkyl group,

a C₁-C₃-haloalkyl group,

25 a C₁-C₃-alkoxy group,

a phenyl group, and

a piperazinyl group, which is optionally substituted with a C(O)R⁶ group,

wherein

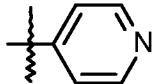
R⁶ is a C₁-C₄-alkyl group,;

30 a thiazol-2-yl group, which is optionally substituted one or two times and each substituent is independently selected from

a C₁-C₄-alkyl group,

- a phenyl group which itself is optionally further substituted with a halogen atom or a C₁-C₃-haloalkyl group; and
- a -CH₂-phenyl group which itself is optionally further substituted with a cyano group;
- 5 a pyrazol-5-yl group, which is optionally substituted one or more times with a C₁-C₄-alkyl group or a phenyl group which itself is optionally substituted with a halogen atom;
- a benzofuran-3-yl group, which is optionally substituted with a C(O)NR⁴R⁵ group,;
- 10 a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen atom; and
- an indazol-7-yl group which is optionally substituted one or more substituents and each substituent independently selected from a halogen atom, a C₁-C₃-alkyl group, a C₁-C₃-haloalkyl group;
- 15 with the proviso that
- 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
- 1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
- 1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
- 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
- 20 1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
- 1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;
- or a stereoisomer, a tautomer, an N-oxide, a hydrate, a solvate, or a salt, a salt of a stereoisomer, a salt of a tautomer, a salt of an N-oxide, a salt of a hydrate, a salt of a solvate, or a mixture of same.

- 25 In accordance with a fourth embodiment of the first aspect, the present invention covers compounds of general formula (I), *supra*, in which:

A  is a group which is optionally substituted by R² and/or R³;

R¹ is a hydrogen atom;

R² is a halogen atom;

- 30 R³ is a hydrogen atom;

- B is a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from
- a halogen atom,
 - a C₁-C₃-alkyl group,
 - 5 a C₁-C₃-haloalkyl group, and
 - a C₁-C₃-alkoxy group;
 - a cyano group,
 - a heteroaryl group,
- is a pyridinyl group,
- 10 which is optionally substituted with one or more substituents and each substituent is independently selected from
- a halogen atom,
 - a cyano group,
 - a C₁-C₃-alkyl group,
 - 15 a C₁-C₃-haloalkyl group,
 - a C₁-C₃-alkoxy group,
 - a phenyl group, and
 - a piperazinyl group, which is optionally substituted with a C(O)R⁶ group,
- wherein
- 20 R⁶ is a C₁-C₄-alkyl group;
- with the proviso that
- 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
 - 1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
 - 1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
 - 25 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
 - 1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
 - 1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;
- or a stereoisomer, a tautomer, an N-oxide, a hydrate, a solvate, or a salt, a salt of a stereoisomer, a salt of a tautomer, a salt of an N-oxide, a salt of a hydrate, a salt of a
- 30 solvate, or a mixture of same.

In accordance with a fifth embodiment of the first aspect, the present invention covers compounds of general formula (I), *supra* which are selected from the group consisting of

- 1-(2-fluoropyridin-4-yl)-3-[2-(trifluoromethyl)pyridin-4-yl]urea,
- 1-(2-chloro-6-methylpyridin-4-yl)-3-(2-chloropyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-[2-chloro-6-(trifluoromethyl)pyridin-4-yl]urea,
1-(2-chloropyridin-4-yl)-3-[4-hydroxy-3-(trifluoromethyl)phenyl]urea,
1-(3-chloro-4-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloro-6-methoxypyridin-4-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3,4-dichlorophenyl)urea,
1,3-bis(2,6-dichloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2,6-dichloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-phenylpyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(6-chloropyridin-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3-cyano-4-fluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(6-chloropyridin-3-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-fluoropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-cyclopropylpyridin-4-yl)urea,
1,3-bis(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-methoxypyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3-cyanophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(4-methylphenyl)urea,
1-(4-chlorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-isoquinolin-6-ylurea,
1-(3-chloro-2-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloro-4-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(3-chloro-4-cyanophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-chloro-3-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-tert-butyl-1,3-thiazol-2-yl)-3-(2-chloropyridin-4-yl)urea,
1-(3-tert-butyl-1-methyl-1H-pyrazol-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3,4,5-trifluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3,5-trifluorophenyl)urea,
1-(2-chloro-3-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,

1-(2-chloro-5-hydroxyphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoro-1H-indazol-7-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoropyrazolo[1,5-a]pyridin-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-hydroxy-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3-dihydro-1H-inden-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3-ethylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3-fluoro-4-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3,5-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2-fluoro-4-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(5-chloropyridin-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2,4-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoro-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2-ethylpyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-7-yl)urea,
1-(2-chloropyridin-4-yl)-3-(6-cyanopyridin-3-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-cyano-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-[3-(trifluoromethyl)phenyl]urea,
1-(2-chloro-3,4-difluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3,4,5-tetrafluorophenyl)urea,
3-[[[(2-chloropyridin-4-yl)carbamoyl]amino]-1-benzofuran-2-carboxamide,
1-(2-chloropyridin-4-yl)-3-[4-methyl-3-(trifluoromethyl)phenyl]urea,
1-(4-chloropyrazolo[1,5-a]pyridin-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-[3,3'-bipyridin]-6-yl-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[4-fluoro-3-(trifluoromethyl)phenyl]urea,
1-(4-bromo-2-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[4-chloro-3-(trifluoromethyl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[2-fluoro-3-(trifluoromethyl)phenyl]urea,

1-(2-chloropyridin-4-yl)-3-[3-fluoro-4-(trifluoromethyl)phenyl]urea,
1-(4-bromo-3-cyanophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-bromo-6-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[4-(4-fluorophenyl)-1,3-thiazol-2-yl]urea,
1-(2-bromo-3-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[1-methyl-5-(trifluoromethyl)-1H-indazol-3-yl]urea,
1-(4-bromo-3,5-difluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-bromo-3-methoxyphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[5-(3-cyanobenzyl)-1,3-thiazol-2-yl]urea,
1-(2-chloropyridin-4-yl)-3-[2-methyl-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl]urea,
1-(2-chloropyridin-4-yl)-3-[2-methoxy-4-(methylsulfonyl)phenyl]urea,
4-[[2-(2-chloropyridin-4-yl)carbamoyl]amino]-N-(1,3-thiazol-2-yl)benzamide,
1-(1-bromoisoquinolin-3-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[3-(pentafluoro-lambda⁶-sulfanyl)phenyl]urea,
1-[4-(3-bromophenyl)-1H-pyrazol-5-yl]-3-(2-chloropyridin-4-yl)urea,
N-(3-[[2-(2-chloropyridin-4-yl)carbamoyl]amino]phenyl)piperidine-1-carboxamide,
1-(2-chloropyridin-4-yl)-3-{4-methyl-3-[2-(morpholin-4-yl)ethoxy]phenyl}urea,
3-bromo-5-[[2-(2-chloropyridin-4-yl)carbamoyl]amino]-N-methylbenzamide,
1-[4-bromo-3-(trifluoromethyl)phenyl]-3-(2-chloropyridin-4-yl)urea,
1-[4-(4-bromophenyl)-1,3-thiazol-2-yl]-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[3-(morpholin-4-ylsulfonyl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-{5-[3-(trifluoromethyl)phenyl]-1,3,4-thiadiazol-2-yl}urea,
1-(2-chloropyridin-4-yl)-3-[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-{2-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]pyridin-4-yl}urea and
1-(3-chlorophenyl)-3-(2-chloropyridin-4-yl)urea

with the proviso that

- 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
5 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a
stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a
5 mixture of same.

In accordance with a another embodiment of the first aspect, the present invention covers
compounds of general formula (I), *supra* which are selected from the group consisting of

1-(2-chloropyridin-4-yl)-3-[4-hydroxy-3-(trifluoromethyl)phenyl]urea,
1-(3-chloro-4-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3,4-dichlorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3-cyano-4-fluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3-cyanophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(4-methylphenyl)urea,
1-(4-chlorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-isoquinolin-6-ylurea,
1-(3-chloro-2-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloro-4-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(3-chloro-4-cyanophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-chloro-3-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-tert-butyl-1,3-thiazol-2-yl)-3-(2-chloropyridin-4-yl)urea,
1-(3-tert-butyl-1-methyl-1H-pyrazol-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3,4,5-trifluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3,5-trifluorophenyl)urea,
1-(2-chloro-3-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloro-5-hydroxyphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoro-1H-indazol-7-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoropyrazolo[1,5-a]pyridin-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-hydroxy-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3-dihydro-1H-inden-5-yl)urea,

1-(2-chloropyridin-4-yl)-3-(3-ethylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3-fluoro-4-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3,5-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2-fluoro-4-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2,4-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoro-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-7-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-cyano-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-[3-(trifluoromethyl)phenyl]urea,
1-(2-chloro-3,4-difluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3,4,5-tetrafluorophenyl)urea,
3-[[[(2-chloropyridin-4-yl)carbamoyl]amino]-1-benzofuran-2-carboxamide,
1-(2-chloropyridin-4-yl)-3-[4-methyl-3-(trifluoromethyl)phenyl]urea,
1-(4-chloropyrazolo[1,5-a]pyridin-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[4-fluoro-3-(trifluoromethyl)phenyl]urea,
1-(4-bromo-2-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[4-chloro-3-(trifluoromethyl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[2-fluoro-3-(trifluoromethyl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[3-fluoro-4-(trifluoromethyl)phenyl]urea,
1-(4-bromo-3-cyanophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-bromo-6-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[4-(4-fluorophenyl)-1,3-thiazol-2-yl]urea,
1-(2-bromo-3-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[1-methyl-5-(trifluoromethyl)-1H-indazol-3-yl]urea,
1-(4-bromo-3,5-difluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-bromo-3-methoxyphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[5-(3-cyanobenzyl)-1,3-thiazol-2-yl]urea,

1-(2-chloropyridin-4-yl)-3-[2-methyl-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl]urea,
 1-(2-chloropyridin-4-yl)-3-[2-methoxy-4-(methylsulfonyl)phenyl]urea,
 4-[[2-(2-chloropyridin-4-yl)carbamoyl]amino]-N-(1,3-thiazol-2-yl)benzamide,
 1-(1-bromoisoquinolin-3-yl)-3-(2-chloropyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-[3-(pentafluoro-lambda⁶-sulfanyl)phenyl]urea,
 1-[4-(3-bromophenyl)-1H-pyrazol-5-yl]-3-(2-chloropyridin-4-yl)urea,
 N-(3-[[2-(2-chloropyridin-4-yl)carbamoyl]amino]phenyl)piperidine-1-carboxamide,
 1-(2-chloropyridin-4-yl)-3-{4-methyl-3-[2-(morpholin-4-yl)ethoxy]phenyl}urea,
 3-bromo-5-[[2-(2-chloropyridin-4-yl)carbamoyl]amino]-N-methylbenzamide,
 1-[4-bromo-3-(trifluoromethyl)phenyl]-3-(2-chloropyridin-4-yl)urea,
 1-[4-(4-bromophenyl)-1,3-thiazol-2-yl]-3-(2-chloropyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-[3-(morpholin-4-ylsulfonyl)phenyl]urea,
 1-(2-chloropyridin-4-yl)-3-{5-[3-(trifluoromethyl)phenyl]-1,3,4-thiadiazol-2-yl}urea,
 1-(2-chloropyridin-4-yl)-3-[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]urea,

with the proviso that

- 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
- 1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
- 1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
- 5 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
- 1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
- 1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

- or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.
- 10

In accordance with another embodiment of the first aspect, the present invention covers compounds of general formula (I), *supra* which are selected from the group consisting of

1-(2-fluoropyridin-4-yl)-3-[2-(trifluoromethyl)pyridin-4-yl]urea
 1-(2-chloro-6-methylpyridin-4-yl)-3-(2-chloropyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-[2-chloro-6-(trifluoromethyl)pyridin-4-yl]urea,
 1-(2-chloro-6-methoxypyridin-4-yl)-3-(2-chloropyridin-4-yl)urea,
 1,3-bis(2,6-dichloropyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(2,6-dichloropyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(2-phenylpyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(6-chloropyridin-2-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(6-chloropyridin-3-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(2-fluoropyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(2-cyclopropylpyridin-4-yl)urea,
 1,3-bis(2-chloropyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(2-methoxypyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(3-chloropyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(5-chloropyridin-2-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(2-ethylpyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(6-cyanopyridin-3-yl)urea,
 1-[3,3'-bipyridin]-6-yl-3-(2-chloropyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-{2-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]pyridin-4-yl}urea and
 1-(3-chlorophenyl)-3-(2-chloropyridin-4-yl)urea

with

the proviso that

- 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
 5 1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
 1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

- or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a
 10 stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a
 mixture of same.

In accordance with a further embodiment of the first aspect, the present invention covers compounds of general formula (I), *supra* which are selected from the group consisting of

1-(2-chloropyridin-4-yl)-3-[4-hydroxy-3-(trifluoromethyl)phenyl]urea,
 1-(3-chloro-4-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(3,4-dichlorophenyl)urea,

1-(2-chloropyridin-4-yl)-3-(3-cyano-4-fluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3-cyanophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(4-methylphenyl)urea,
1-(4-chlorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluorophenyl)urea,
1-(3-chloro-2-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloro-4-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(3-chloro-4-cyanophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-chloro-3-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3,4,5-trifluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3,5-trifluorophenyl)urea,
1-(2-chloro-3-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloro-5-hydroxyphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-hydroxy-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3-ethylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3-fluoro-4-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3,5-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2-fluoro-4-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,4-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoro-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(4-cyano-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-[3-(trifluoromethyl)phenyl]urea,
1-(2-chloro-3,4-difluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3,4,5-tetrafluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-[4-methyl-3-(trifluoromethyl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[4-fluoro-3-(trifluoromethyl)phenyl]urea,
1-(4-bromo-2-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[4-chloro-3-(trifluoromethyl)phenyl]urea,

1-(2-chloropyridin-4-yl)-3-[2-fluoro-3-(trifluoromethyl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[3-fluoro-4-(trifluoromethyl)phenyl]urea,
1-(4-bromo-3-cyanophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-bromo-6-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[4-(4-fluorophenyl)-1,3-thiazol-2-yl]urea,
1-(2-bromo-3-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-bromo-3,5-difluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-bromo-3-methoxyphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[2-methoxy-4-(methylsulfonyl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[3-(pentafluoro-lambda⁶-sulfanyl)phenyl]urea,
N-(3-[[2-chloropyridin-4-yl]carbamoyl]amino)phenyl)piperidine-1-carboxamide,
1-(2-chloropyridin-4-yl)-3-{4-methyl-3-[2-(morpholin-4-yl)ethoxy]phenyl}urea,
3-bromo-5-[[2-chloropyridin-4-yl]carbamoyl]amino}-N-methylbenzamide,
1-[4-bromo-3-(trifluoromethyl)phenyl]-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[3-(morpholin-4-ylsulfonyl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]urea,

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In accordance with a further embodiment of the first aspect, the present invention covers
5 compounds of general formula (I), *supra* which are selected from the group consisting of

1-(2-chloropyridin-4-yl)-3-isoquinolin-6-ylurea,
1-(4-tert-butyl-1,3-thiazol-2-yl)-3-(2-chloropyridin-4-yl)urea,
1-(3-tert-butyl-1-methyl-1H-pyrazol-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoro-1H-indazol-7-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoropyrazolo[1,5-a]pyridin-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3-dihydro-1H-inden-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-7-yl)urea,
3-[[2-chloropyridin-4-yl]carbamoyl]amino}-1-benzofuran-2-carboxamide,

1-(4-chloropyrazolo[1,5-a]pyridin-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[1-methyl-5-(trifluoromethyl)-1H-indazol-3-yl]urea,
1-(2-chloropyridin-4-yl)-3-[5-(3-cyanobenzyl)-1,3-thiazol-2-yl]urea,
1-(2-chloropyridin-4-yl)-3-[2-methyl-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl]urea,
4-[(2-chloropyridin-4-yl)carbamoyl]amino}-N-(1,3-thiazol-2-yl)benzamide,
1-(1-bromoisoquinolin-3-yl)-3-(2-chloropyridin-4-yl)urea,
1-[4-(3-bromophenyl)-1H-pyrazol-5-yl]-3-(2-chloropyridin-4-yl)urea,
1-[4-(4-bromophenyl)-1,3-thiazol-2-yl]-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-{5-[3-(trifluoromethyl)phenyl]-1,3,4-thiadiazol-2-yl}urea,

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In accordance with a further embodiment of the first aspect, the present invention covers
5 compounds of general formula (I), *supra* which are selected from the group consisting of

1-(2-chloropyridin-4-yl)-3-isoquinolin-6-ylurea,
1-(3-tert-butyl-1-methyl-1H-pyrazol-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoro-1H-indazol-7-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoropyrazolo[1,5-a]pyridin-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3-dihydro-1H-inden-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-7-yl)urea,
3-[(2-chloropyridin-4-yl)carbamoyl]amino}-1-benzofuran-2-carboxamide,
1-(4-chloropyrazolo[1,5-a]pyridin-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[1-methyl-5-(trifluoromethyl)-1H-indazol-3-yl]urea,
1-(2-chloropyridin-4-yl)-3-[2-methyl-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl]urea,
1-(1-bromoisoquinolin-3-yl)-3-(2-chloropyridin-4-yl)urea,
1-[4-(3-bromophenyl)-1H-pyrazol-5-yl]-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-{5-[3-(trifluoromethyl)phenyl]-1,3,4-thiadiazol-2-yl}urea,

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In accordance with a further embodiment of the first aspect, the present invention covers compounds of general formula (I), *supra* which are selected from the group consisting of

1-(4-tert-butyl-1,3-thiazol-2-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[5-(3-cyanobenzyl)-1,3-thiazol-2-yl]urea,
4-[(2-chloropyridin-4-yl)carbamoyl]amino}-N-(1,3-thiazol-2-yl)benzamide,
1-[4-(4-bromophenyl)-1,3-thiazol-2-yl]-3-(2-chloropyridin-4-yl)urea,

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In accordance with a further embodiment of the first aspect, the present invention covers compounds of general formula (I), *supra* which are selected from the group consisting of

1-(2-chloropyridin-4-yl)-3-isoquinolin-6-ylurea,
1-(2-chloropyridin-4-yl)-3-(4-fluoro-1H-indazol-7-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoropyrazolo[1,5-a]pyridin-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3-dihydro-1H-inden-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-7-yl)urea,
3-[(2-chloropyridin-4-yl)carbamoyl]amino}-1-benzofuran-2-carboxamide,
1-(4-chloropyrazolo[1,5-a]pyridin-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[1-methyl-5-(trifluoromethyl)-1H-indazol-3-yl]urea,
1-(1-bromoisoquinolin-3-yl)-3-(2-chloropyridin-4-yl)urea,

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

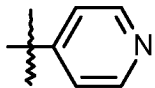
In accordance with a further embodiment of the first aspect, the present invention covers compounds of general formula (I), *supra* which are selected from the group consisting of

1-(4-tert-butyl-1,3-thiazol-2-yl)-3-(2-chloropyridin-4-yl)urea,
1-(3-tert-butyl-1-methyl-1H-pyrazol-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[5-(3-cyanobenzyl)-1,3-thiazol-2-yl]urea,
1-(2-chloropyridin-4-yl)-3-[2-methyl-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl]urea,

4-[(2-chloropyridin-4-yl)carbamoyl]amino}-N-(1,3-thiazol-2-yl)benzamide,
 1-[4-(3-bromophenyl)-1H-pyrazol-5-yl]-3-(2-chloropyridin-4-yl)urea,
 1-[4-(4-bromophenyl)-1,3-thiazol-2-yl]-3-(2-chloropyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-{5-[3-(trifluoromethyl)phenyl]-1,3,4-thiadiazol-2-yl}urea,

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

- 5 In accordance with a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of general formula (I), *supra*, in which:

A is a  group which is optionally substituted by R² and/or R³;

R¹ is a hydrogen atom;

10 R² is a chlorine atom;

R³ is a hydrogen atom;

B a phenyl group, which is substituted with one or more substituents and each substituent is independently selected from

15 a halogen atom,
 a C₁-C₃-alkyl group,
 a C₁-C₃-haloalkyl group,
 a C₁-C₃-alkoxy group,
 a cyano group,
 a heteroaryl group,

20 is a pyridinyl group,
 which is substituted with one or more substituents and each substituent is independently selected from

25 a halogen atom,
 a cyano group,
 a C₁-C₃-alkyl group,
 a C₁-C₃-haloalkyl group,
 a C₁-C₃-alkoxy group,

a phenyl group, and

a piperazinyl group, which is optionally substituted with a C(O)R⁶ group,
wherein

R⁶ is a C₁-C₄-alkyl group;

5 with the proviso that

1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,

1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,

1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,

10 1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and

1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

15 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

R¹ is a hydrogen atom or a methyl group or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

20 In another embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

R¹ is a hydrogen atom or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

25 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

A is a pyridinyl group, more particularly a 3- or 4-pyridinyl group, even more particularly a 4-pyridinyl group, or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

30

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

A is a pyridinyl group which is substituted by a halogen atom, more particularly a 3- or 4-pyridinyl group which are substituted by a halogen atom, even more particularly a 4-

pyridinyl group which is substituted by a halogen atom; or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

5 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

A is a pyridinyl group which is substituted by a fluorine atom or a chlorine atom, more particularly a 3- or 4-pyridinyl group which are substituted by a fluorine atom or a chlorine atom, even more particularly a 4-pyridinyl group which is substituted by a fluorine atom or a chlorine atom, or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof,
10 or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

A is a pyridinyl group which is substituted by a chlorine atom, more particularly a 3- or 4-
15 pyridinyl group which are substituted by a chlorine atom, even more particularly a 4-pyridinyl group which is substituted by a chlorine atom, or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the
20 present invention covers compounds of formula (I), *supra*, in which:

R² is a fluorine atom or a chlorine atom, particularly a chlorine atom, or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the
25 present invention covers compounds of formula (I), *supra*, in which:

R² is a chlorine atom, or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the
30 present invention covers compounds of formula (I), *supra*, in which:

R² is a fluorine atom, or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the
35 present invention covers compounds of formula (I), *supra*, in which:

R³ is a hydrogen atom, a halogen atom or a C₁-C₃-alkyl group or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same..

5 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

R³ is a hydrogen atom or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

10 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

R³ is a halogen atom or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same..

15 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

R³ is a C₁-C₃-alkyl group or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

20 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

R³ is a hydrogen atom or a halogen atom or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

25 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

R³ is a hydrogen atom, or a C₁-C₃-alkyl group or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

30 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

R³ is a halogen atom or a C₁-C₃-alkyl group or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

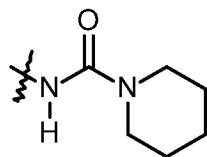
R² is a fluorine atom or a chlorine atom, particularly a chlorine atom, and R³ is a hydrogen atom, or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same..

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

B is

- 10 a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom,
 a C₁-C₃-alkyl group,
 a C₁-C₃-haloalkyl group,
 15 a C₁-C₃-alkoxy group,
 a cyano group,
 a hydroxy group,
 a SF₅ group,
 a -S(O)₂-(C₁-C₃-alkyl) group,
 20 a N(O)₂ group,
 a heteroaryl group,
 a heterocycloalkyl group,
 a -O-(C₁-C₃-alkyl)-heterocycloalkyl,
 a -S(O)₂-heterocycloalkyl group,



- 25 a group and
 a C(O)NR⁴R⁵, wherein

R⁴ is a hydrogen atom or a C₁-C₃-alkyl group; and

R⁵ is a hydrogen atom, a C₁-C₃-alkyl group, or a heteroaryl group;

a pyridinyl group,

- 30 which is optionally substituted with one or more substituents and each substituent is independently selected from
 a halogen atom,

- a cyano group,
a C₁-C₃-alkyl group,
a C₁-C₃-haloalkyl group,
a C₁-C₃-alkoxy group,
5 a C₃-C₆-cycloalkyl group
a phenyl group, which is optionally substituted with a halogen atom, a C₁-C₃-alkyl
group, C₁-C₃-alkoxy group, a CN group, a NR⁴R⁵ group;
a heteroaryl group and
10 a piperazinyl group, which is optionally substituted with a C(O)R⁶ group,
wherein
R⁶ is a C₁-C₄-alkyl group;
a pyrimidinyl group which is optionally substituted with a C₁-C₃-alkyl group or a
piperazinyl group which itself is optionally further substituted with a C₁-C₃-
15 alkyl group;
a thiazolyl group, which is optionally substituted one or two times and each
substituent is independently selected from
a C₁-C₄-alkyl group,
a phenyl group which itself is optionally further substituted with a halogen
20 atom or a C₁-C₃-haloalkyl group, and
a -CH₂-phenyl group which itself is optionally further substituted with a cyano
group;
a pyrazolyl group, which is optionally substituted one or more times with a C₁-C₄-
alkyl group or a phenyl group which itself is optionally substituted with a
25 halogen atom;
a thiadiazolyl group which is optionally substituted with a phenyl group which itself
is optionally substituted with a C₁-C₃-haloalkyl group, or a phenyl group which
itself is optionally substituted with a halogen atom or a C₁-C₃-haloalkyl group;
a benzofuran-3-yl group, which is optionally substituted with a C(O)NR⁴R⁵ group;
30 a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen
atom;
an indazolyl group which is optionally substituted one or more substituents and
each substituent independently selected from a halogen atom, a C₁-C₃-alkyl
group, a C₁-C₃-haloalkyl group;

an isoquinolinyl group which is optionally substituted with a halogen atom; and
a dihydroindenyl group;

with the proviso that

- 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
5 1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;
10 or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a
stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a
mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the
present invention covers compounds of formula (I), *supra*, in which:

- 15 B is

a phenyl group, which is optionally substituted with one or more substituents and
each substituent is independently selected from
a halogen atom,
a C₁-C₃-alkyl group,
20 a C₁-C₃-haloalkyl group,
a C₁-C₃-alkoxy group,
a cyano group,
a heteroaryl group,
a heterocycloalkyl group, a C(O)NR⁴R⁵, wherein

- 25 R⁴ is a hydrogen atom or a C₁-C₃-alkyl group;

R⁵ is a hydrogen atom, a C₁-C₃-alkyl group, a heteroaryl group
a -(C₁-C₃-alkyl)-O-heteroaryl group;

a pyridinyl group,

- which is optionally substituted with one or more substituents and each
30 substituent is independently selected from
a halogen atom,
a cyano group,
a C₁-C₃-alkyl group,
a C₁-C₃-haloalkyl group,

a C₁-C₃-alkoxy group,
a phenyl group, a heteroaryl group, and
a piperazinyl group, which is optionally substituted with a C(O)R⁶ group,
wherein

5 R⁶ is a C₁-C₄-alkyl group;

a pyrimidinyl group which is optionally substituted with a C₁-C₃-alkyl group, or a
piperazinyl group which itself is optionally further substituted with a C₁-C₃-
alkyl group;

10 a thiazol-2-yl group, which is optionally substituted one or two times and each
substituent is independently selected from
a C₁-C₄-alkyl group,
a phenyl group which itself is optionally further substituted with a halogen
atom or a C₁-C₃-haloalkyl group, and
15 a -CH₂-phenyl group which itself is optionally further substituted with a cyano
group;

a pyrazol-5-yl group, which is optionally substituted one or more times with a C₁-
C₄-alkyl group or a phenyl group which itself is optionally substituted with a
halogen atom;

a benzofuran-3-yl group, which is optionally substituted with a C(O)NR⁴R⁵ group;

20 a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen
atom; and

an indazol-7-yl group which is optionally substituted one or more substituents and
each substituent independently selected from a halogen atom, a C₁-C₃-alkyl
group, a C₁-C₃-haloalkyl group,

25 with the proviso that

1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,

1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,

1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,

30 1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and

1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a
stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a
mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

B is

a phenyl group, which is optionally substituted with one or more substituents and each
5 substituent is independently selected from

- a halogen atom,
- a C₁-C₃-alkyl group,
- a C₁-C₃-haloalkyl group,
- a C₁-C₃-alkoxy group,
- 10 a cyano group,
- a heteroaryl group,

is a pyridinyl group,

which is optionally substituted with one or more substituents and each
substituent is independently selected from

- 15 a halogen atom,
- a cyano group,
- a C₁-C₃-alkyl group,
- a C₁-C₃-haloalkyl group,
- a C₁-C₃-alkoxy group,
- 20 a phenyl group, and

a piperazinyl group, which is optionally substituted with a C(O)R⁶ group,
wherein

R⁶ is a C₁-C₄-alkyl group;

a thiazol-2-yl group, which is optionally substituted one or two times and each
25 substituent is independently selected from

- a C₁-C₄-alkyl group,
- a phenyl group which itself is optionally further substituted with a halogen
atom or a C₁-C₃-haloalkyl group, and
- a -CH₂-phenyl group which itself is optionally further substituted with a cyano
30 group;

a pyrazol-5-yl group, which is optionally substituted one or more times with a C₁-
C₄-alkyl group or a phenyl group which itself is optionally substituted with a
halogen atom,

a benzofuran-3-yl group, which is optionally substituted with a C(O)NR⁴R⁵ group;

a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen atom; and

an indazol-7-yl group which is optionally substituted one or more substituents and each substituent independently selected from a halogen atom, a C₁-C₃-alkyl group, a C₁-C₃-haloalkyl group;

with the proviso that

1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,

1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,

10 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and

1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

B is

a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom,

a C₁-C₃-alkyl group,

a C₁-C₃-haloalkyl group, and

a C₁-C₃-alkoxy group,

a cyano group,

a heteroaryl group,

is a pyridinyl group,

which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom,

a cyano group,

a C₁-C₃-alkyl group,

a C₁-C₃-haloalkyl group,

a C₁-C₃-alkoxy group,

a phenyl group, and

a piperazinyl group, which is optionally substituted with a C(O)R⁶ group,
wherein

R⁶ is a C₁-C₄-alkyl group;

with the proviso that

- 5 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
10 1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

- In a further embodiment of the first aspect or any embodiment derived therefrom, the
15 present invention covers compounds of formula (I), *supra*, in which:

B is

a phenyl group, which is optionally substituted with one or more substituents and each
substituent is independently selected from

- 20 a halogen atom,
a C₁-C₃-alkyl group,
a C₁-C₃-haloalkyl group,
a C₁-C₃-alkoxy group,
a cyano group,
a hydroxy group,
25 a heteroaryl group and
a heterocycloalkyl group, a C(O)NR⁴R⁵, wherein

R⁴ is a hydrogen atom or a C₁-C₃-alkyl group;

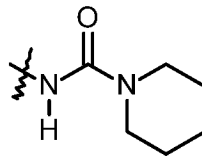
R⁵ is a hydrogen atom, a C₁-C₃-alkyl group, a heteroaryl group
a -(C₁-C₃-alkyl)-O-heteroaryl group;

- 30 more particularly where each substituent is selected from
a halogen atom,
a C₁-C₃-alkyl group,
a C₁-C₃-haloalkyl group,

a C₁-C₃-alkoxy group,
a cyano group, and
a hydroxy group

even more particularly where each substituent is selected from

5 a fluorine atom, a chlorine atom, a bromine atom, a methyl group, an ethyl group, a trifluoromethyl group, a cyano group, a hydroxy group, a nitro group, a pentafluorosulfanyl group, a sulfono-methyl group, a oxadiazolone group, a morpholino group, a -O-(CH₂)₂-morpholino group, a -S(O)₂-



10 morpholino group, a group, a C(O)NH₂ group, a C(O)NH(CH₃) group, a C(O)NH(thiazolyl) group,

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, a salt of a stereoisomer, a salt of a tautomer, a salt of a hydrate, a salt of a solvate, or a mixture of same.

15 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

B is

a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from

20 a halogen atom,
a C₁-C₃-alkyl group,
a C₁-C₃-haloalkyl group, and
a C₁-C₃-alkoxy group,
a cyano group,
a heteroaryl group,

25 or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, a salt of a stereoisomer, a salt of a tautomer, a salt of a hydrate, a salt of a solvate, or a mixture of same.

In yet a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

30 B is

a phenyl group, which is optionally substituted with one or two substituents selected from the lists disclosed *infra*

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

B is

a pyridinyl group,

which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom,

a cyano group,

a C₁-C₃-alkyl group,

a C₁-C₃-haloalkyl group,

a C₁-C₃-alkoxy group,

a cyano group,

a phenyl group,

a heteroaryl group and

a piperazinyl group, which is optionally substituted with a C(O)R⁶ group, whereby

R⁶ is a C₁-C₄-alkyl group,

more particularly which is optionally substituted with one or more substituents and each substituent is independently selected from

a fluorine atom, a chlorine atom, a cyano group, a methyl group, an ethyl group, a trifluoromethyl group, a methoxy group, a cyclopropyl group, a phenyl group, a 4-(2,2-dimethylpropanoyl)piperazin-1-yl group and a pyridinyl group

with the proviso that

1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,

1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,

1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a
stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a
5 mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the
present invention covers compounds of formula (I), *supra*, in which:

B is

10 a pyrimidinyl group which is optionally substituted with a C₁-C₃-alkyl group, or a
piperazinyl group which itself is optionally further substituted with a C₁-C₃-
alkyl group,

more particularly which is optionally substituted with a methyl group or a
piperazino-methyl group,

15 or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a
stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a
mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the
present invention covers compounds of formula (I), *supra*, in which:

B is

20 a thiazol-2-yl group, which is optionally substituted one or two times and each
substituent is independently selected from
a C₁-C₄-alkyl group,

25 a phenyl group which itself is optionally further substituted with a halogen
atom or a C₁-C₃-haloalkyl group, more particularly which itself is optionally
further substituted with a fluorine atom or a chlorine atom or a trifluoromethyl
group, and

a -CH₂-phenyl group which itself is optionally further substituted with a cyano
group;

30 more particularly which is optionally substituted one or two times and each
substituent is independently selected from a methyl group a tert.-butyl group,
a phenyl group which is itself substituted with a substituent selected from a
fluorine atom, a bromine atom and a trifluoromethyl group, and a benzyl group
which is optionally further substituted with a cyano group

with the proviso that if R² is a chlorine atom and B is a thiazolyl group, it may not be mono-substituted with a methyl group;

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

B is

a pyrazol-5-yl group, which is optionally substituted one or more times with a C₁-C₄-alkyl group or a phenyl group which itself is optionally substituted with a halogen atom,

more particularly which is optionally substituted one or more times with a methyl group, a tert-butyl group or a phenyl group which is optionally substituted with a fluorine atom or a chlorine atom

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

B is

a thiadiazolyl group which is optionally substituted with a phenyl group which itself is optionally substituted with a C₁-C₃-haloalkyl group, or a phenyl group which itself is optionally substituted with a halogen atom or a C₁-C₃-haloalkyl group;

more particularly which is optionally substituted with a phenyl group which itself is substituted with a trifluoromethyl group, or a phenyl group which is substituted with a further phenyl group which itself is substituted with a bromine atom and/or a trifluoromethyl group

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

B is

a benzofuran-3-yl group, which is optionally substituted with a C(O)NR⁴R⁵ group,
more particularly which is optionally substituted with a C(O)NH₂ group

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a
5 stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a
mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the
present invention covers compounds of formula (I), *supra*, in which:

B is

10 a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen
atom;

more particularly which is optionally substituted with a fluorine atom or a chlorine
atom

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a
15 stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a
mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the
present invention covers compounds of formula (I), *supra*, in which:

B is

20 a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen
atom;

more particularly which is optionally substituted with a fluorine atom or a chlorine
atom

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a
25 stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a
mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the
present invention covers compounds of formula (I), *supra*, in which:

B is

an indazol-7-yl group which is optionally substituted one or more substituents and each substituent independently selected from a halogen atom, a C₁-C₃-alkyl group, a C₁-C₃-haloalkyl group,
more particularly which is optionally substituted one or more substituents and
5 each substituent independently selected from a fluorine atom, a methyl group and a trifluoromethyl group

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

10 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

A is a pyridinyl group which is substituted with a chlorine atom and B is a phenyl group which is substituted according to any list disclosed *infra* or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or
15 a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

A is a pyridinyl group which is substituted with a chlorine atom and B is a pyridinyl group which is substituted according to any list disclosed *infra* or a stereoisomer, a tautomer, a
20 hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

R⁴ and R⁵ are independently selected from the group consisting of a hydrogen atom, a
25 C₁-C₃-alkyl group, or a heteroaryl group with the proviso that R⁴ and R⁵ both can not be a heteroaryl group at the same time, or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the
30 present invention covers compounds of formula (I), *supra*, in which:

R⁴ is a hydrogen atom or a C₁-C₃-alkyl group;

R⁵ is a hydrogen atom, a C₁-C₃-alkyl group or a heteroaryl group

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

5 In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

R⁴ is a hydrogen atom or a C₁-C₃-alkyl group;

R⁵ is a hydrogen atom, a C₁-C₃-alkyl group, or a heteroaryl group and at least one of R⁴ and R⁵ is a hydrogen atom,

10 or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

R⁶ is a C₁-C₄-alkyl group, ,

15 or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

In a further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers compounds of formula (I), *supra*, in which:

20 R⁶ is a *tert.*-butyl group or a pyridinyl group,

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

25 In a particular further embodiment of the first aspect or any embodiment derived therefrom, the present invention covers combinations of two or more of the above mentioned embodiments under the heading "further embodiments of the first aspect of the present invention".

The present invention covers any sub-combination within any embodiment or aspect of the present invention of compounds of general formula (I), *supra*.

30 The present invention covers any sub-combination within any embodiment or aspect of the present invention of intermediate compounds of general formula (I).

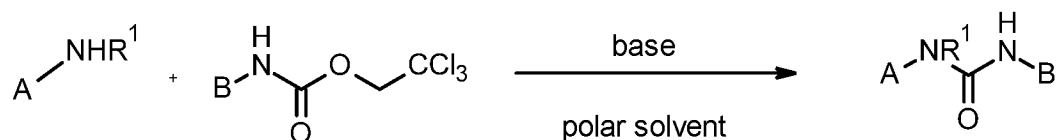
The present invention covers the compounds of general formula (I) which are disclosed in the Example Section of this text, *infra*.

The compounds according to the invention of general formula (I) can be prepared according to the following schemes 1, 2, 3, 4, and 5. The schemes and procedures described below illustrate synthetic routes to the compounds of general formula (I) of the invention and are not intended to be limiting. It is clear to the person skilled in the art that the order of transformations as exemplified in schemes 1, 2, 3, 4, and 5 can be modified in various ways. The order of transformations exemplified in these schemes is therefore not intended to be limiting. In addition, interconversion of any of the substituents, R¹, R², R³, R⁴, R⁵ or R⁶ can be achieved before and/or after the exemplified transformations. These modifications can be such as the introduction of protecting groups, cleavage of protecting groups, reduction or oxidation of functional groups, halogenation, metallation, substitution or other reactions known to the person skilled in the art. These transformations include those which introduce a functionality which allows for further interconversion of substituents. Appropriate protecting groups and their introduction and cleavage are well-known to the person skilled in the art (see for example T.W. Greene and P.G.M. Wuts in *Protective Groups in Organic Synthesis*, 3rd edition, Wiley 1999). Specific examples are described in the subsequent paragraphs.

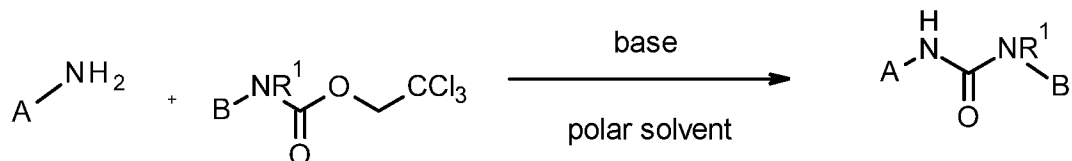
Routes for the preparation of compounds of general formula (I) are described in schemes 1, 2, 3, 4, and 5.

Route 1

a)



b)



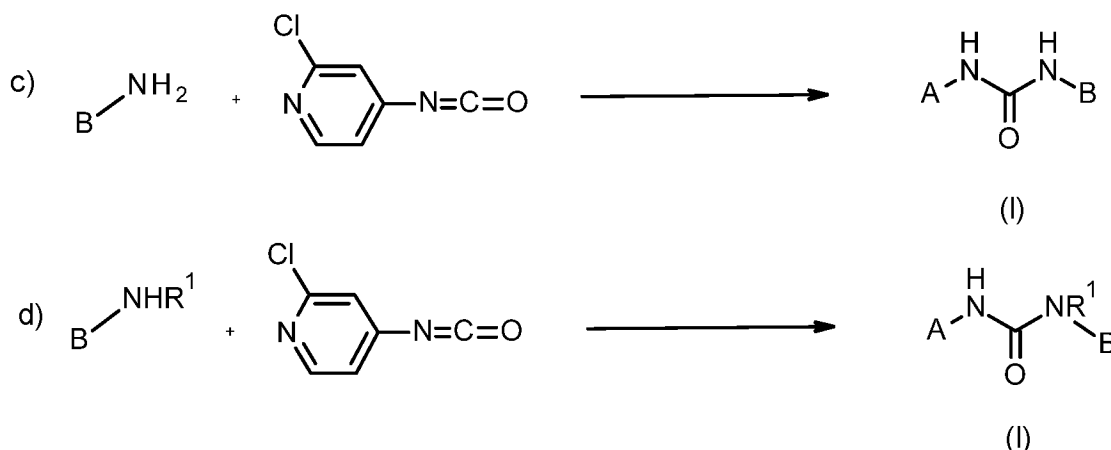
(I)

Scheme 1: Route for the preparation of compounds of general formula (I) in which A and B are pyridine derivatives, but not necessarily identical, A is optionally substituted by R² and/or R³ and whereby B is substituted as defined in any of the claims or aspects or any embodiment derived therefrom *infra* and R¹, R², R³, R⁴, R⁵ and R⁶ have the meaning as given for general formula (I), *supra*.

The starting materials, the respective pyridine amines, are either commercially available or can be prepared according to procedures available from the public domain, as understandable to the person skilled in the art.

A pyridine derivative A-NH₂ or A-NR¹ is dissolved in a suitable solvent, such as e.g. THF, DMF, DMA, DMSO or NMP, in the presence of a base such as e.g. TEA, DIPEA and reacted with a pyridinylcarbamate which optionally substituted with R² and/or R³ and which is dissolved in a polar aprotic solvent such as e.g. THF, DMF, DMA, DMSO or NMP at about 50 - 120°C for up to 2 days. Extraction under usual procedure as known by the skilled person as well as purification by column chromatography leads to a compound of formula I wherein A and B are pyridine derivatives.

Route 2



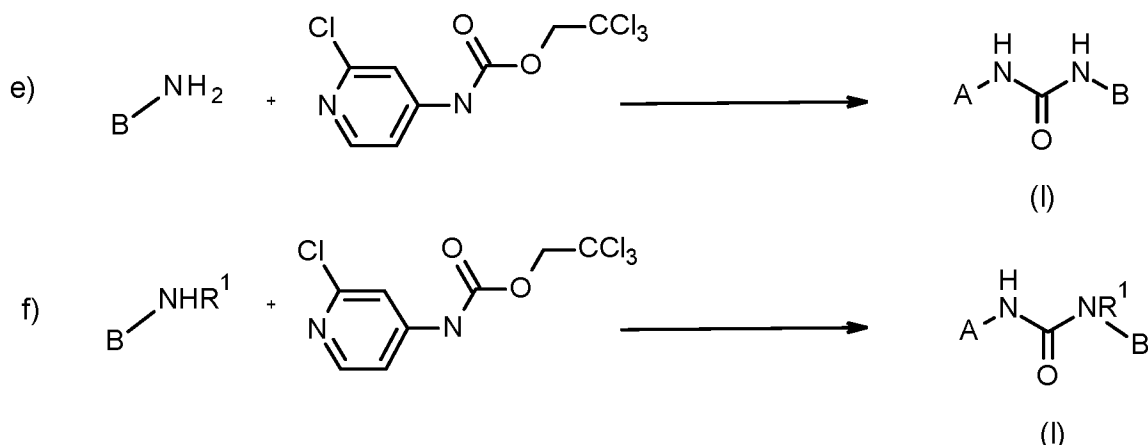
Scheme 2: Route for the preparation of compounds of general formula (I) in which A is e.g. a 2-chloropyridine (as shown above) or a pyridine substituted with one or more substituents and B is a pyridine but not necessarily identical with A, B is optionally substituted as defined in any of the claims or aspects or any embodiment derived therefrom and R¹ is a hydrogen atom or a C₁-C₃-alkyl group such as a methyl group.

The starting materials, the respective pyridine amines, are either commercially available or can be prepared according to procedures available from the public domain, as understandable to the person skilled in the art.

A compound B-NH₂ or B-NH R¹ which is optionally substituted as defined in any of claims 1 to 4 or aspects as defined in the description or any embodiment derived therefrom, is dissolved in a polar aprotic solvent such as e.g. DCM, DMF or NMP and reacted with 2-chloro-4-isocyanatopyridine and a base, such as e.g. an inorganic base, such as e.g. potassium carbonate, caesium carbonate or an organic base, such as e.g. TEA, DIPEA

at room temperature up to 2 days. Usual work-up and purification by column chromatography leads to the compound of formula (I).

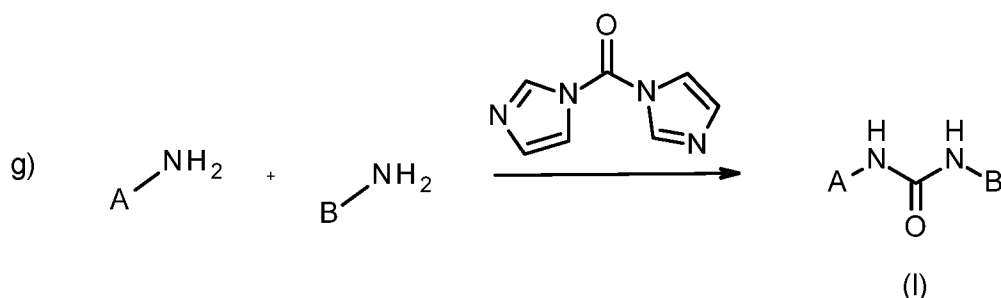
Route 3



Scheme 3: Route for the preparation of compounds of general formula (I) in which A is a 2-chloropyridine and B is a phenyl ring which is substituted with an amino group and which is optionally substituted with further substituents as defined in any of the claims or aspects or any embodiment derived therefrom

- 10 The starting materials, the respective pyridine amines, are either commercially available or can be prepared according to procedures available from the public domain, as understandable to the person skilled in the art.

An aminophenyl derivative which is optionally substituted with further substituents as defined in any of the claims or aspects or any embodiment derived therefrom dissolved
 15 in a polar aprotic solvent such as e.g. THF, DMF, DMA, DMSO or NMP is reacted with a chloropyridinylcarbamate and a suitable organic base such as e.g. TEA or DIPEA at 50°-120°C up to 5 days. Usual work-up and purification leads to a compound of formula (I) wherein B is a phenyl ring.

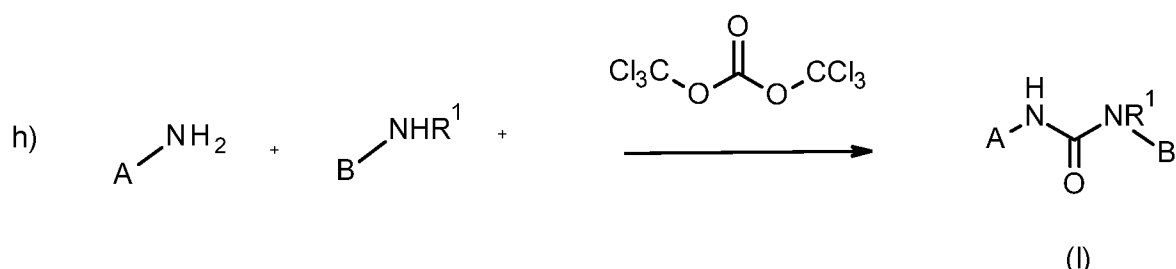
Route 4

Scheme 4: Route for the preparation of compounds of general formula (I) in which A=B and both, A and B, are pyridine rings which are optionally substituted as defined *infra*.

- 5 The starting materials, the respective pyridine amines, are either commercially available or can be prepared according to procedures available from the public domain, as understandable to the person skilled in the art.

In order to obtain symmetrical urea derivatives of formula (I) it is possible to react A-NH₂ with and B-NH₂ with di(1H-imidazol-1-yl)methanone under addition of an organic base such as e.g. TEA or DIPEA in a suitable aprotic organic solvent such as e.g. THF, DMA or NMP at 50-120°C for about 2h. Usual work-up and purification by column chromatography lead to a symmetrical compound of formula (I).

10

Route 5

Scheme 4: Route for the preparation of compounds of general formula (I) in which A and B are pyridine derivatives, but not necessarily identical and are optionally substituted as defined in any of the claims or aspects or any embodiment derived therefrom.

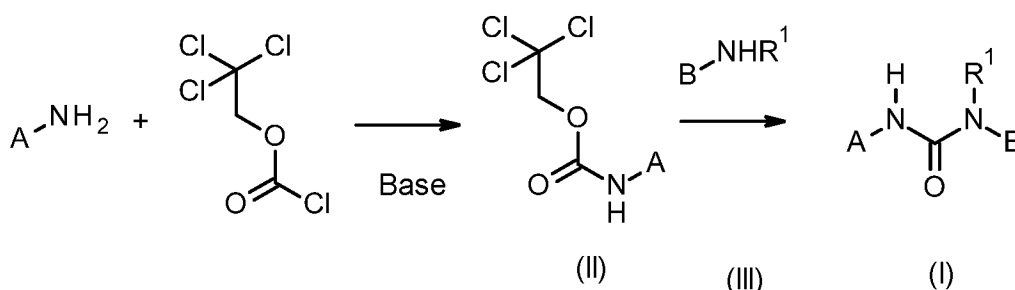
The starting materials, the respective pyridine amines, are either commercially available or can be prepared according to procedures available from the public domain, as understandable to the person skilled in the art.

20

A solution of an amine A-NH₂ in a polar aprotic solvent such as e.g. dichloromethane (DCM), tetrahydrofuran (THF), dimethylformamide (DMF) is reacted with triphosgene

under addition of a suitable organic base such as e.g. triethylamine (TEA) or diisopropylethylamine (DIPEA) at 0°C. After 1h a solution of the second amine B-NHR¹ is added as well as again a suitable organic base such as e.g. TEA or DIPEA at 0°C. A warming up to room temperature was allowed and the mixture stirred overnight, concentrated and purified by column chromatography. A compound of formula (I) wherein A and B are pyridine rings is obtained.

Route 6



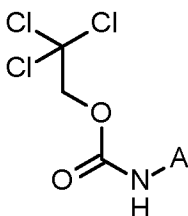
Scheme 5: Route for the preparation of compounds of general formula (I) in which A and B are pyridine derivatives, but not necessarily identical and are optionally substituted as defined in any of the claims or aspects or any embodiment derived therefrom.

The starting materials, the respective pyridine amines, are either commercially available or can be prepared according to procedures available from the public domain, as understandable to the person skilled in the art.

A pyridineamine is reacted with 2,2,2-trichloroethyl carbonochloridate in a polar aprotic solvent such as e.g. dichloromethane (DCM), tetrahydrofuran (THF), dimethylformamide (DMF) in the presence of an amine such as e.g. trimethylamine at 0°C and the mixture stirred for 1 hour at 0°C and additional 3 hours at room temperature. The mixture is filtered and purified by column chromatography.

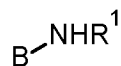
In certain embodiments, R¹ may be hydrogen.

In accordance with a second aspect, the present invention covers methods of preparing compounds of general formula (I) as defined *supra*, said methods comprising the step of allowing an intermediate compound of general formula (II) :



(II),

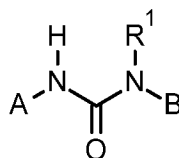
in which A is as defined for the compound of general formula (I) as defined *supra*,
to react with a compound of general formula (III) :



5

(III),

in which B is as defined for the compound of general formula (I) as defined *supra*,
thereby giving a compound of general formula (I) :



(I),

10 in which R¹, A and B are as defined *supra*.

then optionally converting said compound into solvates, salts and/or solvates of such salts using the corresponding (i) solvents and/or (ii) bases or acids.

Specific examples are described in the Experimental Section.

15 The present invention covers methods of preparing compounds of the present invention of general formula (I), said methods comprising the steps as described in the Experimental Section herein.

The compounds of general formula (I) of the present invention can be converted to any salt, preferably pharmaceutically acceptable salts, as described herein, by any method which is known to the person skilled in the art. Similarly, any salt of a compound of general
20 formula (I) of the present invention can be converted into the free compound, by any method which is known to the person skilled in the art.

Compounds of general formula (I) of the present invention have surprisingly been found to effectively inhibit SMARCA2 and it is possible therefore that said compounds be used for the treatment or prophylaxis of diseases, for example, hyperproliferative disorders in
25 humans and animals.

Compounds of the present invention can be utilized to inhibit, block, reduce, decrease, *etc.*, cell proliferation and/or cell division, and/or produce apoptosis. This method comprises administering to a mammal in need thereof, including a human, an amount of

a compound of general formula (I) of the present invention, or a pharmaceutically acceptable salt, isomer, polymorph, metabolite, hydrate, solvate or ester thereof, which is effective to treat the disorder.

Hyperproliferative disorders include, but are not limited to, for example : psoriasis,
5 keloids, and other hyperplasias affecting the skin, benign prostate hyperplasia (BPH), solid tumours, such as cancers of the breast, respiratory tract, brain, reproductive organs, digestive tract, urinary tract, eye, liver, skin, head and neck, thyroid, parathyroid and their distant metastases. Those disorders also include lymphomas, sarcomas, and leukaemias.

10 Examples of breast cancers include, but are not limited to, invasive ductal carcinoma, invasive lobular carcinoma, ductal carcinoma *in situ*, and lobular carcinoma *in situ*.

Examples of cancers of the respiratory tract include, but are not limited to, small-cell and non-small-cell lung carcinoma, as well as bronchial adenoma and pleuropulmonary blastoma.

15 Examples of brain cancers include, but are not limited to, brain stem and hypophtalamic glioma, cerebellar and cerebral astrocytoma, medulloblastoma, ependymoma, as well as neuroectodermal and pineal tumour.

Tumours of the male reproductive organs include, but are not limited to, prostate and testicular cancer.

20 Tumours of the female reproductive organs include, but are not limited to, endometrial, cervical, ovarian, vaginal, and vulvar cancer, as well as sarcoma of the uterus.

Tumours of the digestive tract include, but are not limited to, anal, colon, colorectal, oesophageal, gallbladder, gastric, pancreatic, rectal, small-intestine, and salivary gland cancers.

25 Tumours of the urinary tract include, but are not limited to, bladder, penile, kidney, renal pelvis, ureter, urethral and human papillary renal cancers.

Eye cancers include, but are not limited to, intraocular melanoma and retinoblastoma.

Examples of liver cancers include, but are not limited to, hepatocellular carcinoma (liver cell carcinomas with or without fibrolamellar variant), cholangiocarcinoma (intrahepatic
30 bile duct carcinoma), and mixed hepatocellular cholangiocarcinoma.

Skin cancers include, but are not limited to, squamous cell carcinoma, Kaposi's sarcoma, malignant melanoma, Merkel cell skin cancer, and non-melanoma skin cancer.

Head-and-neck cancers include, but are not limited to, laryngeal, hypopharyngeal, nasopharyngeal, oropharyngeal cancer, lip and oral cavity cancer and squamous cell.

Lymphomas include, but are not limited to, AIDS-related lymphoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, Burkitt lymphoma, Hodgkin's disease, and

5 lymphoma of the central nervous system.

Sarcomas include, but are not limited to, sarcoma of the soft tissue, osteosarcoma, malignant fibrous histiocytoma, lymphosarcoma, and rhabdomyosarcoma.

Leukemias include, but are not limited to, acute myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia, and hairy cell

10 leukemia.

The term "treating" or "treatment" as stated throughout this document is used conventionally, for example the management or care of a subject for the purpose of combating, alleviating, reducing, relieving, stabilizing or improving the condition of a disease or disorder, such as a carcinoma.

15 The compounds of the present invention can be used in particular in therapy and prevention, *i.e.* prophylaxis, of tumour growth and metastases, especially in solid tumours of all indications and stages with or without pre-treatment of the tumour growth.

Generally, the use of chemotherapeutic agents and/or anti-cancer agents in combination with a compound or pharmaceutical composition of the present invention will serve to:

- 20
1. yield better efficacy in reducing the growth of a tumour or even eliminate the tumour as compared to administration of either agent alone,
 2. provide for the administration of lesser amounts of the administered chemotherapeutic agents,
 3. provide for a chemotherapeutic treatment that is well tolerated in the patient with
- 25
- fewer deleterious pharmacological complications than observed with single agent chemotherapies and certain other combined therapies,
 4. provide for treating a broader spectrum of different cancer types in mammals, especially humans,
 5. provide for a higher response rate among treated patients,
- 30
6. provide for a longer survival time among treated patients compared to standard chemotherapy treatments,
 7. provide a longer time for tumour progression, and/or

8. yield efficacy and tolerability results at least as good as those of the agents used alone, compared to known instances where other cancer agent combinations produce antagonistic effects.

In addition, the compounds of general formula (I) of the present invention can also be
5 used in combination with radiotherapy and/or surgical intervention.

In a further embodiment of the present invention, the compounds of general formula (I) of the present invention may be used to sensitize a cell to radiation, *i.e.* treatment of a cell with a compound of the present invention prior to radiation treatment of the cell renders the cell more susceptible to DNA damage and cell death than the cell would be
10 in the absence of any treatment with a compound of the present invention. In one aspect, the cell is treated with at least one compound of general formula (I) of the present invention.

Thus, the present invention also provides a method of killing a cell, wherein a cell is administered one or more compounds of the present invention in combination with
15 conventional radiation therapy.

The present invention also provides a method of rendering a cell more susceptible to cell death, wherein the cell is treated with one or more compounds of general formula (I) of the present invention prior to the treatment of the cell to cause or induce cell death. In one aspect, after the cell is treated with one or more compounds of general formula (I) of
20 the present invention, the cell is treated with at least one compound, or at least one method, or a combination thereof, in order to cause DNA damage for the purpose of inhibiting the function of the normal cell or killing the cell.

In other embodiments of the present invention, a cell is killed by treating the cell with at least one DNA damaging agent, *i.e.* after treating a cell with one or more compounds of
25 general formula (I) of the present invention to sensitize the cell to cell death, the cell is treated with at least one DNA damaging agent to kill the cell. DNA damaging agents useful in the present invention include, but are not limited to, chemotherapeutic agents (*e.g.* cis platin), ionizing radiation (X-rays, ultraviolet radiation), carcinogenic agents, and mutagenic agents.

In other embodiments, a cell is killed by treating the cell with at least one method to cause or induce DNA damage. Such methods include, but are not limited to, activation of a cell signalling pathway that results in DNA damage when the pathway is activated, inhibiting
30 of a cell signalling pathway that results in DNA damage when the pathway is inhibited, and inducing a biochemical change in a cell, wherein the change results in DNA damage.
35 By way of a non-limiting example, a DNA repair pathway in a cell can be inhibited, thereby

preventing the repair of DNA damage and resulting in an abnormal accumulation of DNA damage in a cell.

- In one aspect of the invention, a compound of general formula (I) of the present invention is administered to a cell prior to the radiation or other induction of DNA damage in the cell. In another aspect of the invention, a compound of general formula (I) of the present invention is administered to a cell concomitantly with the radiation or other induction of DNA damage in the cell. In yet another aspect of the invention, a compound of general formula (I) of the present invention is administered to a cell immediately after radiation or other induction of DNA damage in the cell has begun.
- 10 In another aspect, the cell is in vitro. In another embodiment, the cell is in vivo.

- Compounds of the present invention can be utilized to inhibit, block, reduce, decrease, etc., SMARCA2. This method comprises administering to a mammal in need thereof, including a human, an amount of a compound of this invention, or a pharmaceutically acceptable salt, isomer, polymorph, metabolite, hydrate, solvate or ester thereof; which is effective to treat the disorder.
- 15

The present invention also provides methods of treating hyperproliferative disorders, such as cancer disorders.

- These disorders have been well characterized in humans, but also exist with a similar etiology in other mammals, and can be treated by administering pharmaceutical compositions of the present invention.
- 20

- The term "treating" or "treatment" as used in the present text is used conventionally, e.g., the management or care of a subject for the purpose of combating, alleviating, reducing, relieving, stabilizing or improving the condition of a disease or disorder, such as a carcinoma or cancer disorder.
- 25

The compounds of the present invention can be used in particular in therapy of hyperproliferative disorders, e.g., cancer disorders.

- In accordance with a further aspect, the present invention covers compounds of general formula (I), as described *supra*, or stereoisomers, tautomers, N-oxides, hydrates, solvates, and salts thereof, particularly pharmaceutically acceptable salts thereof, or mixtures of same, for use in the treatment or prophylaxis of diseases, in particular hyperproliferative disorders, more particular for cancer disorders.
- 30

The pharmaceutical activity of the compounds according to the invention can be explained by their activity as SMARCA2 inhibitors.

In accordance with a further aspect, the present invention covers the use of compounds of general formula (I), as described *supra*, or stereoisomers, tautomers, N-oxides,
5 hydrates, solvates, and salts thereof, particularly pharmaceutically acceptable salts thereof, or mixtures of same, for the treatment or prophylaxis of diseases, in particular hyperproliferative disorders, particularly cancer disorders.

In accordance with a further aspect, the present invention covers the use of a compound of formula (I), described *supra*, or a stereoisomer, a tautomer, an N-oxide, a hydrate, a
10 solvate, or a salt thereof, particularly a pharmaceutically acceptable salt thereof, or a mixture of same, for the prophylaxis or treatment of diseases, in particular hyperproliferative disorders, particularly cancer disorders.

In accordance with a further aspect, the present invention covers the use of compounds of general formula (I), as described *supra*, or stereoisomers, tautomers, N-oxides,
15 hydrates, solvates, and salts thereof, particularly pharmaceutically acceptable salts thereof, or mixtures of same, in a method of treatment or prophylaxis of diseases, in particular hyperproliferative disorders, particularly cancer disorders.

In accordance with a further aspect, the present invention covers use of a compound of general formula (I), as described *supra*, or stereoisomers, tautomers, N-oxides, hydrates,
20 solvates, and salts thereof, particularly pharmaceutically acceptable salts thereof, or mixtures of same, for the preparation of a pharmaceutical composition, preferably a medicament, for the prophylaxis or treatment of diseases, in particular hyperproliferative disorders, particularly cancer disorders.

In accordance with a further aspect, the present invention covers a method of treatment
25 or prophylaxis of diseases, in particular hyperproliferative disorders, particularly cancer disorders, using an effective amount of a compound of general formula (I), as described *supra*, or stereoisomers, tautomers, N-oxides, hydrates, solvates, and salts thereof, particularly pharmaceutically acceptable salts thereof, or mixtures of same.

In accordance with a further aspect, the present invention covers pharmaceutical
30 compositions, in particular a medicament, comprising a compound of general formula (I), as described *supra*, or a stereoisomer, a tautomer, an N-oxide, a hydrate, a solvate, a salt thereof, particularly a pharmaceutically acceptable salt, or a mixture of same, and one or more excipients), in particular one or more pharmaceutically acceptable excipient(s). Conventional procedures for preparing such pharmaceutical compositions
35 in appropriate dosage forms can be utilized.

The present invention furthermore covers pharmaceutical compositions, in particular medicaments, which comprise at least one compound according to the invention, conventionally together with one or more pharmaceutically suitable excipients, and to their use for the above mentioned purposes.

- 5 It is possible for the compounds according to the invention to have systemic and/or local activity. For this purpose, they can be administered in a suitable manner, such as, for example, via the oral, parenteral, pulmonary, nasal, sublingual, lingual, buccal, rectal, vaginal, dermal, transdermal, conjunctival, otic route or as an implant or stent.

For these administration routes, it is possible for the compounds according to the
10 invention to be administered in suitable administration forms.

For oral administration, it is possible to formulate the compounds according to the invention to dosage forms known in the art that deliver the compounds of the invention rapidly and/or in a modified manner, such as, for example, tablets (uncoated or coated
15 tablets, for example with enteric or controlled release coatings that dissolve with a delay or are insoluble), orally-disintegrating tablets, films/wafers, films/lyophilisates, capsules (for example hard or soft gelatine capsules), sugar-coated tablets, granules, pellets, powders, emulsions, suspensions, aerosols or solutions. It is possible to incorporate the compounds according to the invention in crystalline and/or amorphised and/or dissolved form into said dosage forms.

20 Parenteral administration can be effected with avoidance of an absorption step (for example intravenous, intraarterial, intracardial, intraspinal or intralumbal) or with inclusion of absorption (for example intramuscular, subcutaneous, intracutaneous, percutaneous or intraperitoneal). Administration forms which are suitable for parenteral administration are, inter alia, preparations for injection and infusion in the form of solutions, suspensions,
25 emulsions, lyophilisates or sterile powders.

Examples which are suitable for other administration routes are pharmaceutical forms for inhalation (e.g., powder inhalers, nebulizers), nasal drops, nasal solutions, nasal sprays; tablets/films/wafers/capsules for lingual, sublingual or buccal administration; suppositories; eye drops, eye ointments, eye baths, ocular inserts, ear drops, ear sprays,
30 ear powders, ear-rinses, ear tampons; vaginal capsules, aqueous suspensions (lotions, mixturae agitandae), lipophilic suspensions, emulsions, ointments, creams, transdermal therapeutic systems (such as, for example, patches), milk, pastes, foams, dusting powders, implants or stents.

The compounds according to the invention can be incorporated into the stated
35 administration forms. This can be effected in a manner known per se by mixing with

pharmaceutically suitable excipients. Pharmaceutically suitable excipients include, inter alia,

- 5 • fillers and carriers (for example, cellulose, microcrystalline cellulose (such as, for example, Avicel[®]), lactose, mannitol, starch, calcium phosphate (such as, for example, Di-Cafos[®])),
- ointment bases (for example, petroleum jelly, paraffins, triglycerides, waxes, wool wax, wool wax alcohols, lanolin, hydrophilic ointment, polyethylene glycols),
- bases for suppositories (for example, polyethylene glycols, cacao butter, hard fat),
- 10 • solvents (for example, water, ethanol, isopropanol, glycerol, propylene glycol, medium chain-length triglycerides, fatty oils, liquid polyethylene glycols, paraffins),
- surfactants, emulsifiers, dispersants or wetters (for example sodium dodecyl sulfate), lecithin, phospholipids, fatty alcohols (such as, for example, Lanette[®]), sorbitan fatty acid esters (such as, for example, Span[®]), polyoxyethylene sorbitan fatty acid esters (such as, for example, Tween[®]), polyoxyethylene fatty acid
- 15 glycerides (such as, for example, Cremophor[®]), polyoxethylene fatty acid esters, polyoxyethylene fatty alcohol ethers, glycerol fatty acid esters, poloxamers (such as, for example, Pluronic[®]),
- buffers, acids and bases (for example, phosphates, carbonates, citric acid, acetic acid, hydrochloric acid, sodium hydroxide solution, ammonium carbonate,
- 20 trometamol, triethanolamine),
- isotonicity agents (for example, glucose, sodium chloride),
- adsorbents (for example, highly-disperse silicas),
- viscosity-increasing agents, gel formers, thickeners and/or binders (for example polyvinylpyrrolidone, methylcellulose, hydroxypropylmethylcellulose,
- 25 hydroxypropylcellulose, carboxymethylcellulose-sodium, starch, carbomers, polyacrylic acids (such as, for example, Carbopol[®]); alginates, gelatine),
- disintegrants (for example, modified starch, carboxymethylcellulose-sodium, sodium starch glycolate (such as, for example, Explotab[®]), cross- linked polyvinylpyrrolidone, croscarmellose-sodium (such as, for example, AcDiSol[®])),

- flow regulators, lubricants, glidants and mould release agents (for example magnesium stearate, stearic acid, talc, highly-disperse silicas (such as, for example, Aerosil®)),
- 5 • coating materials (for example sugar, shellac) and film formers for films or diffusion membranes which dissolve rapidly or in a modified manner (for example polyvinylpyrrolidones (such as, for example, Kollidon®), polyvinyl alcohol, hydroxypropylmethylcellulose, hydroxypropylcellulose, ethylcellulose, hydroxypropylmethylcellulose phthalate, cellulose acetate, cellulose acetate phthalate, polyacrylates, polymethacrylates such as, for example, Eudragit®),
- 10 • capsule materials (for example gelatine, hydroxypropylmethylcellulose),
- synthetic polymers (for example polylactides, polyglycolides, polyacrylates, polymethacrylates (such as, for example, Eudragit®), polyvinylpyrrolidones (such as, for example, Kollidon®), polyvinyl alcohols, polyvinyl acetates, polyethylene oxides, polyethylene glycols and their copolymers and blockcopolymers),
- 15 • plasticizers (for example, polyethylene glycols, propylene glycol, glycerol, triacetine, triacetyl citrate, dibutyl phthalate),
- penetration enhancers,
- stabilisers (for example, antioxidants such as, for example, ascorbic acid, ascorbyl palmitate, sodium ascorbate, butylhydroxyanisole, butylhydroxytoluene, propyl
- 20 gallate),
- preservatives (for example, parabens, sorbic acid, thiomersal, benzalkonium chloride, chlorhexidine acetate, sodium benzoate),
- colourants (for example, inorganic pigments such as, for example, iron oxides, titanium dioxide),
- 25 • flavourings, sweeteners, flavour- and/or odour-masking agents.

The present invention furthermore relates to a pharmaceutical composition which comprises at least one compound according to the invention, conventionally together with one or more pharmaceutically suitable excipient(s), and to their use according to the present invention.

In accordance with another aspect, the present invention covers pharmaceutical combinations, in particular medicaments, comprising at least one compound of general formula (I) of the present invention and at least one or more further active ingredients, in particular for the treatment and/or prophylaxis of a hyperproliferative disease, especially cancer.

Particularly, the present invention covers a pharmaceutical combination, which comprises:

- one or more first active ingredients, in particular compounds of general formula (I) as defined *supra*, and
- one or more further active ingredients, in particular a hyperproliferative disease, especially cancer.

The term “combination” in the present invention is used as known to persons skilled in the art, it being possible for said combination to be a fixed combination, a non-fixed combination or a kit-of-parts.

A “fixed combination” in the present invention is used as known to persons skilled in the art and is defined as a combination wherein, for example, a first active ingredient, such as one or more compounds of general formula (I) of the present invention, and a further active ingredient are present together in one unit dosage or in one single entity. One example of a “fixed combination” is a pharmaceutical composition wherein a first active ingredient and a further active ingredient are present in admixture for simultaneous administration, such as in a formulation. Another example of a “fixed combination” is a pharmaceutical combination wherein a first active ingredient and a further active ingredient are present in one unit without being in admixture.

A non-fixed combination or “kit-of-parts” in the present invention is used as known to persons skilled in the art and is defined as a combination wherein a first active ingredient and a further active ingredient are present in more than one unit. One example of a non-fixed combination or kit-of-parts is a combination wherein the first active ingredient and the further active ingredient are present separately. It is possible for the components of the non-fixed combination or kit-of-parts to be administered separately, sequentially, simultaneously, concurrently or chronologically staggered.

The compounds of the present invention can be administered as the sole pharmaceutical agent or in combination with one or more other pharmaceutically active ingredients where the combination causes no unacceptable adverse effects. The present invention also

covers such pharmaceutical combinations. For example, the compounds of the present invention can be combined with known anti-cancer agents.

Examples of antiproliferative agents, more particularly anti-cancer agents include:

131I-chTNT, abarelix, abemaciclib, abiraterone, acalabrutinib, aclerubicin, adalimumab,
5 ado-trastuzumab emtansine, afatinib, aflibercept, aldesleukin, alectinib, alemtuzumab, alendronic acid, alitretinoin, altretamine, amifostine, aminoglutethimide, hexyl aminolevulinate, amrubicin, amsacrine, anastrozole, anacetim, anethole dithiolethione, anetumab ravtansine, angiotensin II, antithrombin III, apalutamide, aprepitant, arcitumomab, arglabin, arsenic trioxide, asparaginase, atezolizumab, avelumab,
10 axicabtagene ciloleucel, axitinib, azacitidine, basiliximab, belotecan, bendamustine, besilesomab, belinostat, bevacizumab, bexarotene, bicalutamide, bisantrene, bleomycin, blinatumomab, bortezomib, bosutinib, buserelin, brentuximab vedotin, brigatinib, busulfan, cabazitaxel, cabozantinib, calcitonine, calcium folinate, calcium levofolinate, capecitabine, capromab, carbamazepine carboplatin, carboquone, carfilzomib, carmofur,
15 carmustine, catumaxomab, celecoxib, celmoleukin, ceritinib, cetuximab, chlorambucil, chlormadinone, chlormethine, cidofovir, cinacalcet, cisplatin, cladribine, clodronic acid, clofarabine, cobimetinib, copanlisib, crisantaspase, crizotinib, cyclophosphamide, cyproterone, cytarabine, dacarbazine, dactinomycin, daratumumab, darbepoetin alfa, dabrafenib, dasatinib, daunorubicin, decitabine, degarelix, denileukin diftotox,
20 denosumab, depreotide, deslorelin, dianhydrogalactitol, dextrazoxane, dibrospidium chloride, dianhydrogalactitol, diclofenac, dinutuximab, docetaxel, dolasetron, doxifluridine, doxorubicin, doxorubicin + estrone, dronabinol, durvalumab, eculizumab, edrecolomab, elliptinium acetate, elotuzumab, eltrombopag, enasidenib, endostatin, enocitabine, enzalutamide, epirubicin, epitiostanol, epoetin alfa, epoetin beta, epoetin zeta,
25 eptaplatin, eribulin, erlotinib, esomeprazole, estradiol, estramustine, ethinylestradiol, etoposide, everolimus, exemestane, fadrozole, fentanyl, filgrastim, fluoxymesterone, floxuridine, fludarabine, fluorouracil, flutamide, folinic acid, formestane, fosaprepitant, fotemustine, fulvestrant, gadobutrol, gadoteridol, gadoteric acid meglumine, gadoversetamide, gadoxetic acid, gallium nitrate, ganirelix, gefitinib,
30 gemcitabine, gemtuzumab, Glucarpidase, glutoxim, GM-CSF, goserelin, granisetron, granulocyte colony stimulating factor, histamine dihydrochloride, histrelin, hydroxycarbamide, I-125 seeds, lansoprazole, ibandronic acid, ibritumomab tiuxetan, ibrutinib, idarubicin, ifosfamide, imatinib, imiquimod, improsulfan, indisetron, incadronic acid, ingenol mebutate, inotuzumab ozogamicin, interferon alfa, interferon beta,
35 interferon gamma, iobitridol, iobenguane (123I), iomeprol, ipilimumab, irinotecan, Itraconazole, ixabepilone, ixazomib, lanreotide, lansoprazole, lapatinib, lasocholine,

lenalidomide, lenvatinib, lenograstim, lentinan, letrozole, leuprorelin, levamisole, levonorgestrel, levothyroxine sodium, lisuride, lobaplatin, lomustine, lonidamine, lutetium Lu 177 dotatate, masoprocol, medroxyprogesterone, megestrol, melarsoprol, melphalan, mepitiostane, mercaptopurine, mesna, methadone, methotrexate, methoxsalen, 5 methylaminolevulinate, methylprednisolone, methyltestosterone, metirosine, midostaurin, mifamurtide, miltefosine, miriplatin, mitobronitol, mitoguazone, mitolactol, mitomycin, mitotane, mitoxantrone, mogamulizumab, molgramostim, mopidamol, morphine hydrochloride, morphine sulfate, mvasi, nabilone, nabiximols, nafarelin, naloxone + pentazocine, naltrexone, nartogastim, necitumumab, nedaplatin, nelarabine, 10 neratinib, neridronic acid, netupitant/palonosetron, nivolumab, pentetreotide, nilotinib, nilutamide, nimorazole, nimotuzumab, nimustine, nintedanib, niraparib, nitracrine, nivolumab, obinutuzumab, octreotide, ofatumumab, olaparib, olaratumab, omacetaxine mepesuccinate, omeprazole, ondansetron, oprelvekin, orgotein, orilotimod, osimertinib, oxaliplatin, oxycodone, oxymetholone, ozogamicine, p53 gene therapy, paclitaxel, 15 palbociclib, palifermin, palladium-103 seed, palonosetron, pamidronic acid, panitumumab, panobinostat, pantoprazole, pazopanib, pegaspargase, PEG-epoetin beta (methoxy PEG-epoetin beta), pembrolizumab, pegfilgrastim, peginterferon alfa-2b, pembrolizumab, pemetrexed, pentazocine, pentostatin, peplomycin, Perflubutane, perfosfamide, Pertuzumab, picibanil, pilocarpine, pirarubicin, pixantrone, plerixafor, 20 plicamycin, poliglusam, polyestradiol phosphate, polyvinylpyrrolidone + sodium hyaluronate, polysaccharide-K, pomalidomide, ponatinib, porfimer sodium, pralatrexate, prednimustine, prednisone, procarbazine, procodazole, propranolol, quinagolide, rabeprazole, racotumomab, radium-223 chloride, radotinib, raloxifene, raltitrexed, ramosetron, ramucirumab, ranimustine, rasburicase, razoxane, refametinib, regorafenib, 25 ribociclib, risedronic acid, rhenium-186 etidronate, rituximab, rolapitant, romidepsin, romiplostim, romurtide, rucaparib, samarium (153Sm) lexidronam, sargramostim, sarilumab, satumomab, secretin, siltuximab, sipuleucel-T, sizofiran, sobuzoxane, sodium glycididazole, sonidegib, sorafenib, stanozolol, streptozocin, sunitinib, talaporfin, talimogene laherparepvec, tamibarotene, tamoxifen, tapentadol, tasonermin, teceleukin, 30 technetium (99mTc) nofetumomab merpentan, 99mTc-HYNIC-[Tyr3]-octreotide, tegafur, tegafur + gimeracil + oteracil, temoporfin, temozolomide, temsirolimus, teniposide, testosterone, tetrofosmin, thalidomide, thiotepa, thymalfasin, thyrotropin alfa, tioguanine, tisagenlecleucel, tocilizumab, topotecan, toremifene, tositumomab, trabectedin, trametinib, tramadol, trastuzumab, trastuzumab emtansine, treosulfan, tretinoin, 35 trifluridine + tipiracil, trilostane, triptorelin, trametinib, trofosfamide, thrombopoietin, tryptophan, ubenimex, valatinib, valrubicin, vandetanib, vaporeotide, vemurafenib,

vinblastine, vincristine, vindesine, vinflunine, vinorelbine, vismodegib, vorinostat, vorozole, yttrium-90 glass microspheres, zinostatin, zinostatin stimalamer, zoledronic acid, zorubicin.

Based upon standard laboratory techniques known to evaluate compounds useful for the treatment of hyperproliferative disorders, by standard toxicity tests and by standard pharmacological assays for the determination of treatment of the conditions identified above in mammals, and by comparison of these results with the results of known active ingredients or medicaments that are used to treat these conditions, the effective dosage of the compounds of the present invention can readily be determined for treatment of each desired indication. The amount of the active ingredient to be administered in the treatment of one of these conditions can vary widely according to such considerations as the particular compound and dosage unit employed, the mode of administration, the period of treatment, the age and sex of the patient treated, and the nature and extent of the condition treated.

The total amount of the active ingredient to be administered will generally range from about 0.001 mg/kg to about 200 mg/kg body weight per day, and from about 0.01 mg/kg to about 20 mg/kg body weight per day. Clinically useful dosing schedules will range from one to three times a day dosing to once every four weeks dosing. In addition, it is possible for "drug holidays", in which a patient is not dosed with a drug for a certain period of time, to be beneficial to the overall balance between pharmacological effect and tolerability. It is possible for a unit dosage to contain from about 0.5 mg to about 1500 mg of active ingredient, and can be administered one or more times per day or less than once a day. The average daily dosage for administration by injection, including intravenous, intramuscular, subcutaneous and parenteral injections, and use of infusion techniques will be from 0.01 to 200 mg/kg of total body weight. The average daily rectal dosage regimen will be from 0.01 to 200 mg/kg of total body weight. The average daily vaginal dosage regimen will be from 0.01 to 200 mg/kg of total body weight. The average daily topical dosage regimen will be from 0.1 to 200 mg administered between one to four times daily. The transdermal concentration will be that required to maintain a daily dose of from 0.01 to 200 mg/kg. The average daily inhalation dosage regimen will be from 0.01 to 100 mg/kg of total body weight.

Of course the specific initial and continuing dosage regimen for each patient will vary according to the nature and severity of the condition as determined by the attending diagnostician, the activity of the specific compound employed, the age and general condition of the patient, time of administration, route of administration, rate of excretion

of the drug, drug combinations, and the like. The desired mode of treatment and number of doses of a compound of the present invention or a pharmaceutically acceptable salt or ester or composition thereof can be ascertained by those skilled in the art using conventional treatment tests.

5 EXPERIMENTAL SECTION

NMR peak forms are stated as they appear in the spectra, possible higher order effects have not been considered.

Table 1: Abbreviations

The following table lists the abbreviations used herein.

10

Abbreviation	Meaning
ACN	acetonitrile
br	broad (¹ H-NMR signal)
d	doublet
DAD	diode array detector
DCM	dichloromethane
dd	double-doublet
DIPEA	diisopropylethylamine
DMA	<i>N,N</i> -dimethylacetamide
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethylsulfoxide
dt	double-triplet
eq.	equivalent
ESI	electrospray (ES) ionisation
h	hour(s)
HPLC	high performance liquid chromatography
LC-MS	liquid chromatography mass spectrometry
M	Molar
m	multiplet
min	minute(s)
MS	mass spectrometry
NMR	nuclear magnetic resonance spectroscopy: chemical shifts (δ) are given in ppm. The chemical shifts were

Abbreviation	Meaning
	corrected by setting the DMSO signal to 2.50 ppm unless otherwise stated.
NMP	N-methylpyrrolidone
ppm	parts per million
q	quartet
r.t. or rt or RT	room temperature
rac	racemic
R _t or R _t	retention time (as measured either with HPLC or UPLC) in minutes
s	singulet
t	triplet
TEA	triethylamine
THF	tetrahydrofuran
TOF	Time of flight
UPLC	ultra performance liquid chromatography
UV	Ultraviolet

Other abbreviations have their meanings customary per se to the skilled person.

The various aspects of the invention described in this application are illustrated by the following examples which are not meant to limit the invention in any way.

The example testing experiments described herein serve to illustrate the present invention and the invention is not limited to the examples given.

EXPERIMENTAL SECTION - GENERAL PART

All reagents, for which the synthesis is not described in the experimental part, are either commercially available, or are known compounds or may be formed from known compounds by known methods by a person skilled in the art. The Examples are intended to illustrate but not to limit the disclosure. Additional compounds not specifically exemplified may be synthesized using conventional methods in combination with the methods described herein.

The compounds and intermediates produced according to the methods of the invention may require purification. Purification of organic compounds is well known to the person skilled in the art and there may be several ways of purifying the same compound. In some cases, no purification may be necessary. In some cases, the compounds may be purified

by crystallization. In some cases, impurities may be stirred out using a suitable solvent. In some cases, the compounds may be purified by chromatography, particularly flash column chromatography, using for example prepacked silica gel cartridges, e.g. Biotage SNAP cartridges KP-Sil® or KP-NH® in combination with a Biotage autopurifier system (SP4® or Isolera Four®) and eluents such as gradients of hexane/ethyl acetate or DCM/methanol. In some cases, the compounds may be purified by preparative HPLC using for example a Waters autopurifier equipped with a diode array detector and/or on-line electrospray ionization mass spectrometer in combination with a suitable prepacked reverse phase column and eluents such as gradients of water and acetonitrile which may contain additives such as trifluoroacetic acid, formic acid or aqueous ammonia.

In some cases, purification methods as described above can provide those compounds of the present invention which possess a sufficiently basic or acidic functionality in the form of a salt, such as, in the case of a compound of the present invention which is sufficiently basic, a trifluoroacetate or formate salt for example, or, in the case of a compound of the present invention which is sufficiently acidic, an ammonium salt for example. A salt of this type can either be transformed into its free base or free acid form, respectively, by various methods known to the person skilled in the art, or be used as salts in subsequent biological assays. It is to be understood that the specific form (e.g. salt, free base etc.) of a compound of the present invention as isolated and as described herein is not necessarily the only form in which said compound can be applied to a biological assay in order to quantify the specific biological activity.

Analytical LC-MS methods:

Method 1:

Instrument: Waters Acquity UPLCMS SingleQuad; Column: Acquity UPLC BEH C18 1.7 µm, 50x2.1mm; eluent A: water + 0.2 vol % aqueous ammonia (32%), eluent B: acetonitrile; gradient: 0-1.6 min 1-99% B, 1.6-2.0 min 99% B; flow 0.8 ml/min; temperature: 60 °C; DAD scan: 210-400 nm.

Method 2

Instrument: Waters Acquity UPLCMS SingleQuad; Column: Acquity UPLC BEH C18 1.7 50x2.1mm; eluent A: water + 0.1 vol % formic acid (99%), eluent B: acetonitrile; gradient: 0-1.6 min 1-99% B, 1.6-2.0 min 99% B; flow 0.8 ml/min; temperature: 60 °C; DAD scan: 210-400 nm.

Method 3

Instrument: Waters Acquity UPLCMS SingleQuad; Colum: Acquity UPLC BEH C18 1.7 50x2.1mm; eluent A: water + 0.2 vol % aqueous ammonia (32%), eluent B: acetonitrile; gradient: 0-1.6 min 1-99% B, 1.6-2.0 min 99% B; flow 0.8 ml/min; temperature: 60 °C; DAD scan: 210-400 nm.

5 Method 4

Instrument: Waters Acquity UPLCMS Single Quad; column: Kinetex 2.6 µm, 50x2.1mm; Eluent A: water + 0.05 % formic acid (99%); Eluent B: acetonitrile + 0.05 % formic acid (99%); gradient: 0-1.9 1-99% B, 1.9-2.1 99% B; flow 1.3 ml/min; temperature: 60°C; DAD scan: 200-400 nm.

10 Method 5

Instrument: Agilent 1290 UPLCMS 6230 TOF; column: BEH C 18 1.7 µm, 50x2.1mm; Eluent A: water + 0.05 % formic acid (99%); Eluent B: acetonitrile + 0.05 % formic acid (99%); gradient: 0-1.7 2-90% B, 1.7-2.0 90% B; flow 1.2 ml/min; temperature: 60°C; DAD scan: 190-400 nm.

15 **Preparative HPLC High Throughput**

Method A

Instrument: Waters Autopurification MS SingleQuad; Colum: Waters XBrigde C18 5µ 100x30mm; eluent A: water + 0.2 vol % aqueous ammonia (32%), eluent B: acetonitrile; gradient: 0-5.5 min 5-100% B; flow 70 ml/min; temperature: 25 °C; DAD scan: 210-400 nm.

20

Method B

Instrument: Waters Autopurification MS SingleQuad; Column: Waters XBrigde C18 5µ 100x30mm; eluent A: water + 0.1 vol % formic acid (99%), eluent B: acetonitrile; gradient: 0-5.5 min 5-100% B; flow 70 ml/min; temperature: 25 °C; DAD scan: 210-400 nm.

25 **Method C**

Instrument: pump: Labomatic HD-5000 or HD-3000, head HDK 280, lowpressure gradient module ND-B1000; manual injection valve: Rheodyne 3725i038; detector: Knauer Azura UVD 2.15; collector: Labomatic Labocol Vario-4000; column: Chromatorex RP C-18 10 µm, 125x30mm; eluent: see specific example; gradient: see specific example; flow 150 ml/min; UV-Detection see specific example.

30

Eluent acidic: solvent A: water + 0.1 vol-% formic acid, solvent B: acetonitrile.

Eluent basic: solvent A: water + 0.2 vol-% ammonia (32%), solvent B: acetonitrile.

Gradient 1: 0.00-0.50 min 15% B, 0.50–6.00 min 15-55% B, 6.00-6.10 min 55-100% B, 6.10-8.00 min 100% B.

Gradient 2: 0.00-0.50 min 30% B, 0.50–6.00 min 30-70% B, 6.00-6.10 min 70-100% B, 6.10-8.00 min 100% B.

5 Method D

Instrument: Waters Autopurification MS SingleQuad; Column: YMC Actus Triart C18 100x30 mm; DAD scan: 210-400 nm; eluent A: water + 0.1 % ammonia (33%), eluent B: acetonitrile (ACN); gradient (60ml/min) according to retention time from LC-MS method 1:

min	
0.00	Start %ACN
0.20	Start %ACN
4.10	End %ACN
4.30	to 99%B
5.50	99%B
6.00	10%B

10

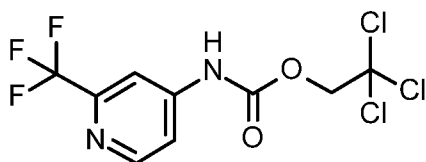
Retention time LC-MS		Eluent		Runtime
from Rt (min)	to Rt (min)	Start (% ACN)	End (% ACN)	(min)
0.00	0.30	1	10	6
0.30	0.52	1	20	6
0.52	0.56	5	35	6
0.56	0.64	10	40	6
0.64	0.70	15	45	6
0.70	0.81	20	50	6
0.81	0.91	25	55	6
0.91	0.97	30	60	6
0.97	1.10	35	65	6
1.10	1.15	40	70	6
1.15	1.22	45	75	6
1.22	1.24	50	80	6
1.24	1.26	55	85	6
1.26	1.28	60	90	6
1.28	1.39	65	99	6
1.39	1.54	70	99	6

1.54	2.00	80	99	6
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EXPERIMENTAL SECTION – INTERMEDIATES

5 Intermediate 1

2,2,2-Trichloroethyl [2-(trifluoromethyl)pyridin-4-yl]carbamate



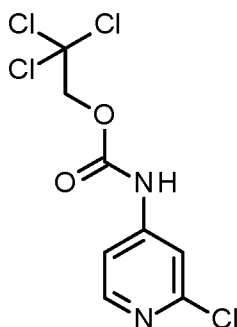
2.0 g (12.3 mmol) 2-(trifluoromethyl)pyridin-4-amine and 1.7 ml (12.3 mmol) triethylamine in 24 ml dichloromethane were cooled to 0°C. 1.8 ml (13 mmol) 2,2,2-trichloroethyl carbonochloridate were added at 0 °C and the mixture stirred for 1h at 0°C and at rt for 3 days. The precipitate formed was filtered off and the organic solvent evaporated. The residue was purified by column chromatography (silica gel, hexane/ ethyl acetate gradient) to give 3.18 g of the title compound.

LC-MS (method 1): $R_t = 1.25$ min; MS (ESI+): $m/z = 339$ $[M+H]^+$.

15

Intermediate 2

2,2,2-Trichloroethyl (2-chloropyridin-4-yl)carbamate



20 In analogy to the synthesis of intermediate 1, 15.20 g (33.4 mmol) 2-chloropyridin-4-amine, 4.8 ml (35 mmol) 2,2,2-trichloroethyl carbonochloridate and 4.7 ml (33 mmol)

trimethylamine in 65 ml dichloromethane gave after purification by column chromatography (silica gel, hexane/ ethyl acetate gradient) 26.54 g of the title compound.

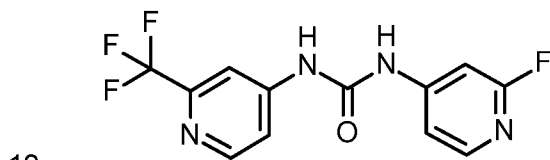
^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ ppm 5.00 (s, 2 H), 7.35 - 7.51 (m, 1 H), 7.59 (d, $J=1.77$ Hz, 1 H), 8.27 (d, $J=5.83$ Hz, 1 H), 10.77 - 11.01 (m, 1 H).

5 LC-MS (method 1): R_t = 1.18 min; MS (ESI+): m/z = 305 $[\text{M}+\text{H}]^+$.

EXPERIMENTAL SECTION – EXAMPLES

Example 1

1-(2-fluoropyridin-4-yl)-3-[2-(trifluoromethyl)pyridin-4-yl]urea



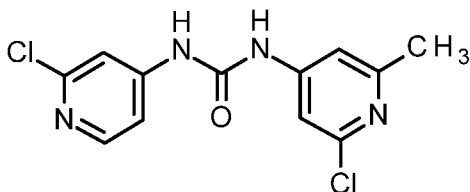
A mixture of 664 mg (5.93 mmol) 2-fluoropyridin-4-amine, 2.5 ml (18 mmol) triethylamine was stirred at room temperature for 30 min, 2.00 g (5.93 mmol) intermediate 1 dissolved in 20 ml N-methylpyrrolidone were added and heated to 60°C for 2 days. The reaction mixture was extracted with ethyl acetate, the combined organic layers dried with sodium sulfate and the solvent evaporated. The residue was purified by column chromatography (silica gel, hexane/ ethyl acetate gradient) followed by preparative HPLC (method A) to give 34.0 mg of the title compound.

15 ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ ppm 7.30 (s, 2 H), 7.56 - 7.70 (m, 1 H), 7.96 - 8.12 (m, 2 H), 8.58 (d, $J=5.58$ Hz, 1 H), 9.82 (d, $J=9.38$ Hz, 2 H)

20 LC-MS (method 3): R_t = 0.94 min; MS (ESI+): m/z = 301 $[\text{M}+\text{H}]^+$.

Example 2

1-(2-chloro-6-methylpyridin-4-yl)-3-(2-chloropyridin-4-yl)urea



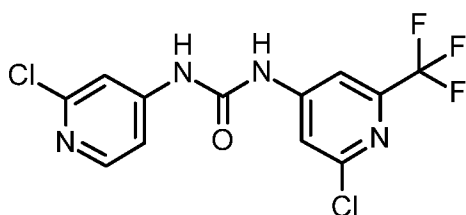
92.3 mg (647 μ mol) 2-chloro-6-methylpyridin-4-amine in 3.0 ml dichloromethane was treated with 100.0 mg (647 μ mol) 2-chloro-4-isocyanatopyridine and 358.0 mg (2.59 mmol) potassium carbonate and stirred at room temperature for 1 day. The solids were filtered off and the solvent evaporated. The residue was purified by column chromatography (silica gel, hexane/ ethyl acetate gradient) followed by preparative HPLC (method A) to give 58.0 mg of the title compound.

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ ppm 2.39 (s, 3 H), 7.22 (d, $J=1.27$ Hz, 1 H), 7.36 (d, $J=5.58$ Hz, 1 H), 7.46 (d, $J=1.77$ Hz, 1 H), 7.65 (d, $J=1.77$ Hz, 1 H), 8.22 (d, $J=5.58$ Hz, 1 H), 9.47 - 9.59 (m, 1 H), 9.62 - 9.72 (m, 1 H).

LC-MS (method 3): R_t = 0.95 min; MS (ESI+): m/z = 299 $[\text{M}+\text{H}]^+$.

Example 3

1-(2-chloropyridin-4-yl)-3-[2-chloro-6-(trifluoromethyl)pyridin-4-yl]urea



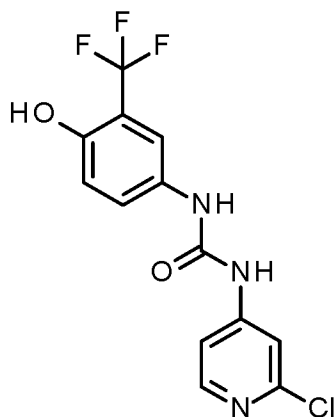
127.0 mg (647 μ mol) 2-chloro-6-(trifluoromethyl)pyridin-4-amine in 3.0 ml N-methylpyrrolidone was treated with 100.0 mg (647 μ mol) 2-chloro-4-isocyanatopyridine and 358.0 mg (2.59 mmol) potassium carbonate and stirred at room temperature for 1 day. The solids were filtered off and the solvent evaporated. The residue was purified by column chromatography (silica gel, hexane/ ethyl acetate gradient) followed by preparative HPLC (method A) to give 14.0 mg of the title compound.

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ ppm 7.41 (s, 1 H) 7.67 (d, $J=1.52$ Hz, 1 H) 7.81 (d, $J=1.27$ Hz, 1 H) 7.97 (d, $J=1.52$ Hz, 1 H) 8.25 (d, $J=5.58$ Hz, 1 H) 9.62 - 10.20 (m, 2 H).

LC-MS (method 3): R_t = 1.14 min; MS (ESI+): m/z = 352 $[\text{M}+\text{H}]^+$.

Example 4

1-(2-chloropyridin-4-yl)-3-[4-hydroxy-3-(trifluoromethyl)phenyl]urea



69.9 mg (395 μ mol) 4-amino-2-(trifluoromethyl)phenol in 1.2 ml N-methylpyrrolidone was treated with 120.0 mg (395 μ mol) intermediate **2** and 110 μ L (790 μ mol) triethylamine and stirred at 80°C for 17 hours. The solvent was evaporated and the residue was purified by preparative HPLC (method A) to give 15.0 mg of the title compound.

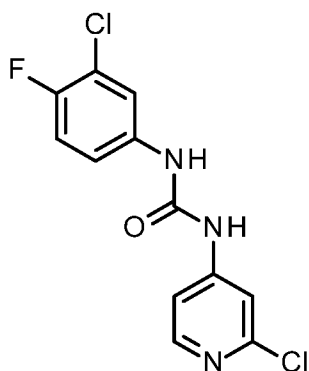
^1H NMR (400 MHz, DMSO- d_6) δ ppm 6.98 (d, J =8.87 Hz, 1 H), 7.32 (dd, J =5.58, 2.03 Hz, 2 H), 7.60 - 7.77 (m, 2 H), 8.17 (d, J =5.58 Hz, 1 H), 8.95 (s, 1 H), 9.37 (s, 1 H), 10.29 (s, 1 H).

LC-MS (method 3): R_t = 0.93 min; MS (ESI+): m/z = 333 $[\text{M}+\text{H}]^+$.

10

Example 5

1-(3-chloro-4-fluorophenyl)-3-(2-chloropyridin-4-yl)urea



113.0 mg (776 μ mol) 3-chloro-4-fluoroaniline, 120.0 mg (776 μ mol) 2-chloro-4-isocyanatopyridine and 220 μ L (1.6 mmol) triethylamine in 2.4 ml N-methylpyrrolidone were stirred at room temperature for 2 day. The solvent was evaporated and the residue purified by preparative HPLC (method C, eluent: basic, gradient: 2, UV detection: 261 nm) to give 100.0 mg of the title compound.

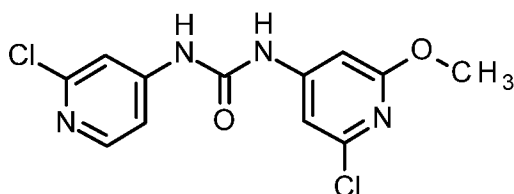
15

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ ppm 7.30 - 7.42 (m, 3 H), 7.64 (d, $J=1.77$ Hz, 1 H), 7.75 - 7.85 (m, 1 H), 8.19 (d, $J=5.83$ Hz, 1 H), 9.20 (s, 1 H), 9.48 (s, 1 H).

LC-MS (method 5): $R_t = 1.08$ min; MS (ESI+): $m/z = 300$ $[\text{M}+\text{H}]^+$.

5 **Example 6**

1-(2-chloro-6-methoxypyridin-4-yl)-3-(2-chloropyridin-4-yl)urea



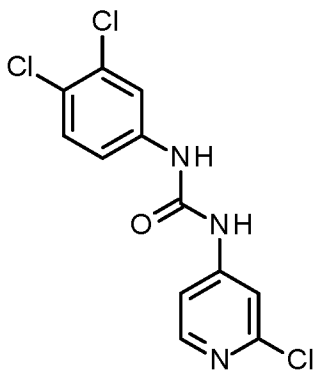
In analogy to example 4, 52.2 mg (329 μmol) 2-chloro-6-methoxypyridin-4-amine, 100.0 mg (329 μmol) intermediate 2 and 183 μL (1.32 mmol) triethylamine in N-methylpyrrolidone at 60°C for 3 days gave 8.0 mg of the title compound after purification by preparative HPLC (method A).

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ ppm 3.82 (s, 3 H), 6.88 (d, $J=1.52$ Hz, 1 H), 7.19 (d, $J=1.27$ Hz, 1 H), 7.30 - 7.44 (m, 1 H), 7.63 (d, $J=1.52$ Hz, 1 H), 8.22 (d, $J=5.58$ Hz, 1 H), 9.61 (s, 1 H), 9.67 (s, 1 H).

LC-MS (method 3): $R_t = 1.08$ min; MS (ESI+): $m/z = 314$ $[\text{M}+\text{H}]^+$.

Example 7

1-(2-chloropyridin-4-yl)-3-(3,4-dichlorophenyl)urea



In analogy to the synthesis of example 5, 126.0 mg (776 μmol) 3,4-dichloroaniline and 120.0 mg (776 μmol) 2-chloro-4-isocyanatopyridine gave 100.0 mg of the title compound

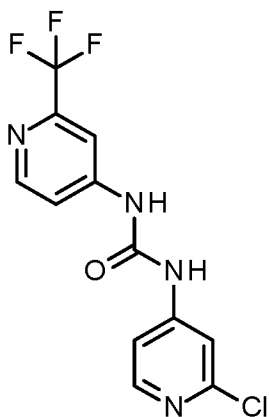
after purification by preparative HPLC (method C, eluent: basic, gradient: 2, UV detection: 261 nm).

¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 7.30 - 7.40 (m, 2 H), 7.56 (d, *J*=8.87 Hz, 1 H), 7.64 (d, *J*=1.77 Hz, 1 H), 7.86 (d, *J*=2.53 Hz, 1 H), 8.20 (d, *J*=5.83 Hz, 1 H), 9.32 (s, 1 H), 9.52 (s, 1 H).

LC-MS (method 5): *R*_t = 1.18 min; MS (ESI⁺): *m/z* = 316 [M+H]⁺.

Example 8

1-(2-chloropyridin-4-yl)-3-[2-(trifluoromethyl)pyridin-4-yl]urea



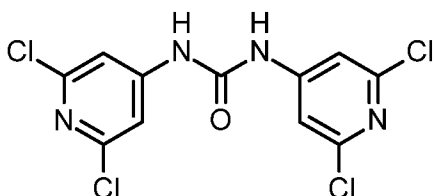
In analogy to example 4, 85.3 mg (526 μmol) 2-(trifluoromethyl)pyridin-4-amine and 160.0 mg (526 μmol) intermediate 2 in N-methylpyrrolidone at 180°C for 2 hours gave 30.0 mg of the title compound after purification by preparative HPLC (method C, eluent: basic, gradient: 2, UV detection: 265 nm).

¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 7.36 - 7.42 (m, 1 H), 7.67 (d, *J*=1.77 Hz, 2 H), 8.05 (d, *J*=2.03 Hz, 1 H), 8.23 (d, *J*=5.58 Hz, 1 H), 8.57 (d, *J*=5.58 Hz, 1 H), 9.84 - 9.95 (m, 1 H), 9.98 - 10.08 (m, 1 H).

LC-MS (method 5): *R*_t = 0.95 min; MS (ESI⁺): *m/z* = 317 [M+H]⁺.

Example 9

1,3-bis(2,6-dichloropyridin-4-yl)urea



A mixture of 180 mg (1.10 mmol) 2,6-dichloropyridin-4-amine and 179 mg (1.10 mmol) di(1H-imidazol-1-yl)methanone in 4.0 ml THF was heated for 30 h at 100 °C in the microwave. 2 Equivalents (2.20 mmol) triethylamine were added and the mixture again stirred for 2 hours at 100 °C in the microwave. The solvents were evaporated and the residue purified by column chromatography (silica gel, hexane/ ethylacetate) to give 117.0 mg of the title compound.

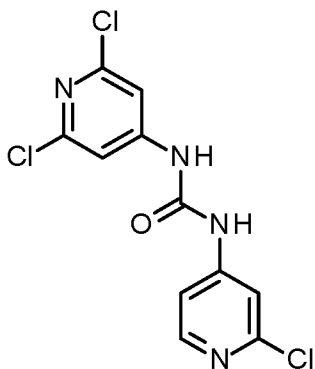
¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 7.58 (s, 2 H), 9.90 - 10.13 (m, 1 H).

LC-MS (method 5): *R*_t = 1.27 min; MS (ESI⁺): *m/z* = 352 [M+H]⁺.

10

Example 10

1-(2-chloropyridin-4-yl)-3-(2,6-dichloropyridin-4-yl)urea

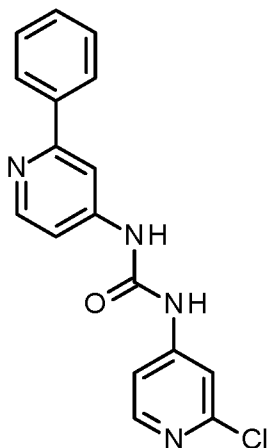


In analogy to example 5, 127.0 mg (776 μmol) 2,6-dichloropyridin-4-amine, 120.0 mg (776 μmol) 2-chloro-4-isocyanatopyridine and 0.22 ml (1.6 mmol) triethylamine in N-methylpyrrolidone at room temperature for 3 days gave 13.0 mg of the title compound after purification by preparative HPLC (method A).

¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 7.32 - 7.44 (m, 1 H), 7.58 (s, 2 H), 7.62 - 7.70 (m, 1 H), 8.14 - 8.32 (m, 1 H), 9.74 - 10.00 (m, 2 H).

LC-MS (method 3): *R*_t = 1.07 min; MS (ESI⁺): *m/z* = 316 [M+H]⁺.

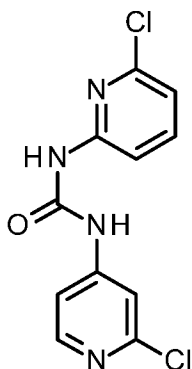
20

Example 11**1-(2-chloropyridin-4-yl)-3-(2-phenylpyridin-4-yl)urea**

In analogy to example 5, 110.0 mg (647 μ mol) 2-phenylpyridin-4-amine, 100.0 mg (647 μ mol) 2-chloro-4-isocyanatopyridine and 0.18 ml (1.3 mmol) triethylamine in 1 N-methylpyrrolidone at room temperature for 17 hours gave 13.0 mg of the title compound after purification by preparative HPLC (method A).

^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ ppm 7.36 - 7.47 (m, 3 H), 7.48 - 7.55 (m, 2 H), 7.70 (d, $J=1.77$ Hz, 1 H), 7.96 - 8.05 (m, 3 H), 8.23 (d, $J=5.83$ Hz, 1 H), 8.50 (d, $J=5.32$ Hz, 1 H), 9.52 (s, 1 H), 9.65 (s, 1 H).

LC-MS (method 3): R_t = 1.11 min; MS (ESI+): m/z = 325 $[\text{M}+\text{H}]^+$.

Example 12**1-(2-chloropyridin-4-yl)-3-(6-chloropyridin-2-yl)urea**

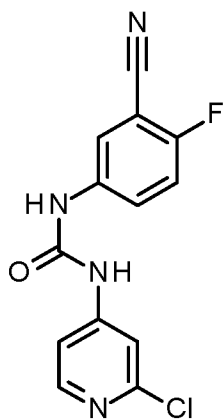
In analogy to example 4, 50.8 mg (395 μ mol) 6-chloropyridin-2-amine and 120.0 mg (395 μ mol) intermediate 2 gave 10.0 mg of the title compound after purification by preparative HPLC (method C, eluent: acidic, gradient: 2, UV detection: 255 nm).

- 5 ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ ppm 7.17 (dd, $J=7.10, 1.27$ Hz, 1 H), 7.33 (dd, $J=5.58, 2.03$ Hz, 1 H), 7.67 (d, $J=1.77$ Hz, 1 H), 7.75 - 7.91 (m, 2 H), 8.23 (d, $J=5.58$ Hz, 1 H), 9.68 - 9.89 (m, 2 H).

LC-MS (method 5): $R_t = 1.00$ min; MS (ESI+): $m/z = 283$ $[\text{M}+\text{H}]^+$.

10 Example 13

1-(2-chloropyridin-4-yl)-3-(3-cyano-4-fluorophenyl)urea



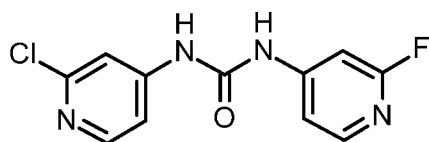
- 15 In analogy to example 4, 53.7 mg (395 μ mol) 5-amino-2-fluorobenzonitrile, 120.0 mg (395 μ mol) intermediate 2 and 0.11 ml (790 μ mol) triethylamine in N-methylpyrrolidone at 60°C for 3 days gave 22.0 mg of the title compound after purification by preparative HPLC (method A).

- 20 ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ ppm 7.32 - 7.37 (m, 1 H), 7.50 (s, 1 H), 7.65 (d, $J=1.52$ Hz, 1 H), 7.72 - 7.81 (m, 1 H), 7.93 - 8.00 (m, 1 H), 8.20 (d, $J=5.83$ Hz, 1 H), 9.29 - 9.39 (m, 1 H), 9.57 (s, 1 H).

LC-MS (method 3): $R_t = 0.99$ min; MS (ESI+): $m/z = 291$ $[\text{M}+\text{H}]^+$.

Example 15

1-(2-chloropyridin-4-yl)-3-(2-fluoropyridin-4-yl)urea



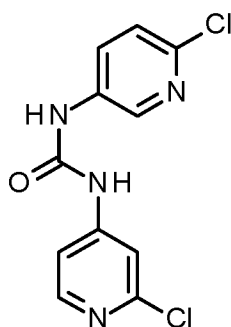
In analogy to example 4, 258.0 mg (2.30 mmol) 2-fluoropyridin-4-amine, 700.0 mg (2.30 mmol) intermediate 2 and 0.64 ml (4.60 mmol) triethylamine in N-methylpyrrolidone at 60°C for 5 days gave 15.0 mg of the title compound after purification by preparative HPLC (method A).

¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 7.29 (q, *J*=1.27 Hz, 2 H), 7.37 (dd, *J*=5.70, 1.90 Hz, 1 H), 7.65 (d, *J*=1.77 Hz, 1 H), 8.07 (d, *J*=6.34 Hz, 1 H), 8.23 (d, *J*=5.58 Hz, 1 H), 9.67 (s, 1 H), 9.75 (s, 1 H).

LC-MS (method 3): *R*_t = 0.85 min; MS (ESI⁺): *m/z* = 267 [M+H]⁺.

Example 14

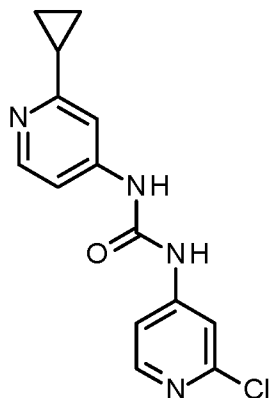
1-(2-chloropyridin-4-yl)-3-(6-chloropyridin-3-yl)urea



In analogy to example 4, 50.8 mg (395 μmol) 6-chloropyridin-3-amine, 120.0 mg (395 μmol) intermediate 2 and 0.17 ml (1.2 mmol) triethylamine in N-methylpyrrolidone at 60°C for 3 days gave 29.0 mg of the title compound after purification by preparative HPLC (method A).

¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 7.33 - 7.38 (m, 1 H), 7.44 - 7.50 (m, 1 H), 7.62 - 7.68 (m, 1 H), 7.90 - 8.02 (m, 1 H), 8.20 (d, *J*=5.58 Hz, 1 H), 8.46 - 8.51 (m, 1 H), 9.34 (s, 1 H), 9.59 (s, 1 H).

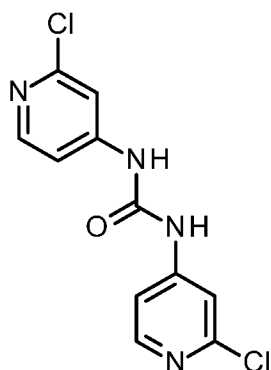
LC-MS (method 3): *R*_t = 0.92 min; MS (ESI⁺): *m/z* = 283 [M+H]⁺.

Example 16**1-(2-chloropyridin-4-yl)-3-(2-cyclopropylpyridin-4-yl)urea**

- 5 In analogy to example 5, 108.0 mg (802 μ mol) 2-cyclopropylpyridin-4-amine, 124.0 mg (802 μ mol) 2-chloro-4-isocyanatopyridine and 0.22 ml (1.60 mmol) triethylamine in N-methylpyrrolidone at room temperature for 1 day gave 20.0 mg of the title compound after purification by preparative HPLC (method B).

¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 0.84 - 0.95 (m, 4 H), 2.01 (s, 1 H), 7.20 (s, 1 H),
10 7.31 - 7.40 (m, 2 H), 7.66 (d, *J*=1.77 Hz, 1 H), 8.21 (d, *J*=5.58 Hz, 2 H), 9.32 - 9.43 (m, 1 H), 9.60 (s, 1 H).

LC-MS (method 2): *R*_t = 0.60 min; MS (ESI⁺): *m/z* = 289 [M+H]⁺.

Example 17**1,3-bis(2-chloropyridin-4-yl)urea**

A mixture of 300 mg (2.33 mmol) 2-chloropyridin-4-amine and 946 mg (5.83 mmol) di(1H-imidazol-1-yl)methanone in 10.0 ml THF was heated at 50 °C for 3 days. The solvent was

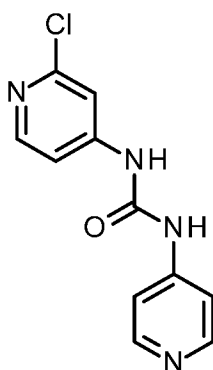
evaporated and the residue purified by preparative HPLC (method C, eluent: basic, gradient: 1, UV detection: 275 nm) to give 105.0 mg of the title compound.

^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ ppm 7.37 (dd, $J=5.70$, 1.90 Hz, 1 H), 7.65 (d, $J=1.52$ Hz, 1 H), 8.23 (d, $J=5.58$ Hz, 1 H), 9.70 (s, 1 H).

- 5 LC-MS (method 4): R_t = 0.83 min; MS (ESI+): m/z = 283 $[\text{M}+\text{H}]^+$.

Example 18

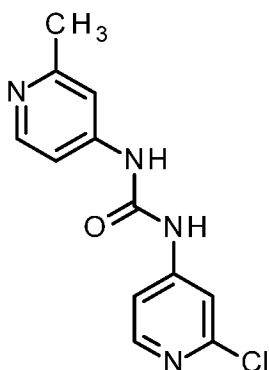
1-(2-chloropyridin-4-yl)-3-pyridin-4-ylurea



- 10 In analogy to example 4, 26.0 mg (276 μmol) pyridin-4-amine, 84.0 mg (276 μmol) intermediate 2 and 77.0 μl (550 μmol) triethylamine in N-methylpyrrolidone at 50°C for 3 days gave 40.0 mg of the title compound after purification by preparative HPLC(method C, eluent: basic, gradient: 1, UV detection: 275 nm).

- ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ ppm 7.29 - 7.39 (m, 1 H), 7.45 (d, $J=6.34$ Hz, 2 H), 7.60
15 - 7.68 (m, 1 H), 8.21 (d, $J=5.58$ Hz, 1 H), 8.40 (d, $J=6.34$ Hz, 2 H), 9.37 - 9.51 (m, 1 H), 9.54 - 9.68 (m, 1 H).

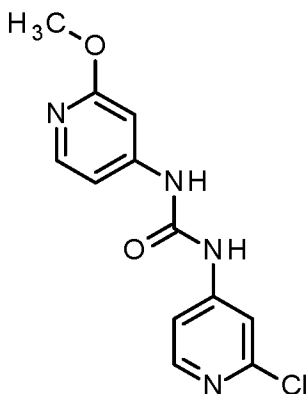
LC-MS (method 4): R_t = 0.40 min; MS (ESI+): m/z = 249 $[\text{M}+\text{H}]^+$.

Example 19**1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea**

- 5 In analogy to example 4, 36.6 mg (329 μ mol) 2-methylpyridin-4-amine, 100.0 mg (329 μ mol) intermediate 2 and 92.0 μ l (660 μ mol) triethylamine in N-methylpyrrolidone at 50°C for 17 hours gave 30.0 mg of the title compound after purification by preparative HPLC (method C, eluent: basic, gradient: 1, UV detection: 249 nm).

- ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 2.41 (s, 3 H), 7.20 - 7.29 (m, 1 H), 7.29 - 7.39 (m, 2 H), 7.66 (d, *J*=1.77 Hz, 1 H), 8.21 (d, *J*=5.58 Hz, 1 H), 8.26 (d, *J*=5.58 Hz, 1 H), 9.34 (s, 1 H), 9.54 (s, 1 H).

LC-MS (method 5): *R*_t = 0.43 min; MS (ESI⁺): *m/z* = 263 [M+H]⁺.

Example 20**15 1-(2-chloropyridin-4-yl)-3-(2-methoxypyridin-4-yl)urea**

In analogy to example 5, 80.3 mg (647 μ mol) 2-methoxypyridin-4-amine, 100.0 mg (647 μ mol) 2-chloro-4-isocyanatopyridine and 180.0 μ l (1.3 mmol) triethylamine in N-

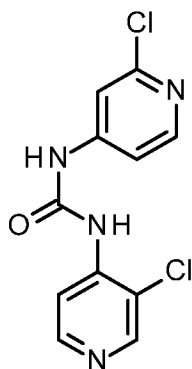
methylpyrrolidone at room temperature for 17 hours gave 45.0 mg of the title compound after purification by preparative HPLC (method C, eluent: acidic, gradient: 1, UV detection: 276 nm).

¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 3.81 (s, 3 H), 6.98 (d, *J*=0.76 Hz, 2 H), 7.29 - 7.41 (m, 1 H), 7.64 (d, *J*=1.77 Hz, 1 H), 8.00 (d, *J*=6.08 Hz, 1 H), 8.21 (d, *J*=5.83 Hz, 1 H), 9.52 (s, 1 H), 9.66 (s, 1 H).

LC-MS (method 5): *R*_t = 0.63 min; MS (ESI⁺): *m/z* = 279 [M+H]⁺.

Example 21

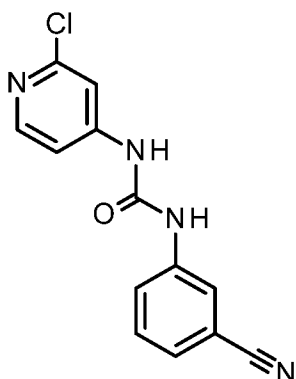
10 1-(2-chloropyridin-4-yl)-3-(3-chloropyridin-4-yl)urea



To a solution of 200 mg (1.6 mmol) 2-chloropyridin-4-amine in 30 mL of dichloromethane were added 0.7 mL of triethylamine and 232 mg (0.8 mmol) triphosgene at 0 °C. The resulting mixture was stirred at 0 °C for 1 hour. 200 mg (1.6 mmol) 3-chloropyridin-4-amine were added. The resulting mixture was stirred at 0 °C for 0.5 hours, and 0.7 ml of triethylamine were added. The resulting mixture was stirred and warmed to room temperature overnight. Upon completion of the reaction, the solvent was removed in vacuo and the residue was purified by preparative HPLC (Column: Gemini-NX/5u, C18 150*21.2mm ; Mobile Phase A: water (10mMol/L ammonium hydrogen carbonate), 15 Mobile Phase B: acetonitrile; Flow rate: 20 mL/min; Gradient: 18% B to 55% B in 8 min; 20 254 & 220 nm *R*_t: 7.83 min) to give 115.2 mg of the title compound.

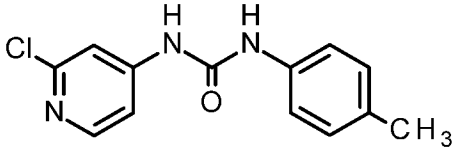
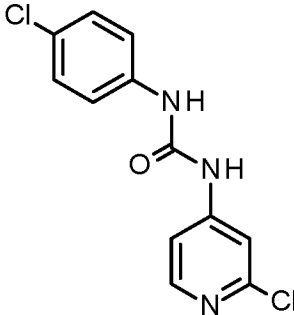
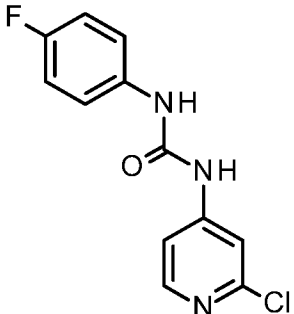
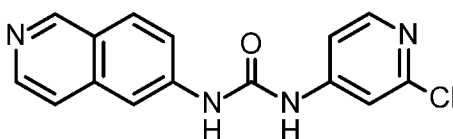
¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 7.19 - 7.36 (m, 1 H), 7.59 - 7.73 (m, 1 H), 8.17 - 8.28 (m, 2 H), 8.32 - 8.44 (m, 1 H), 8.50 - 8.59 (m, 1 H), 8.75 - 8.98 (m, 1 H), 10.15 - 10.37 (m, 1 H).

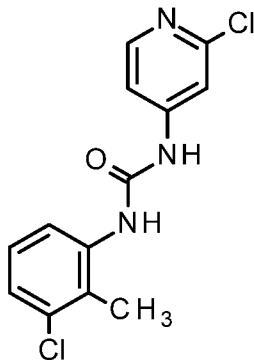
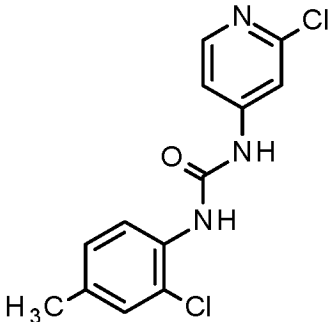
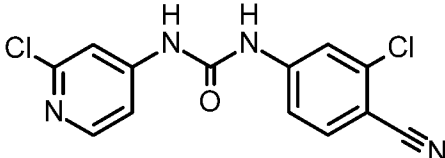
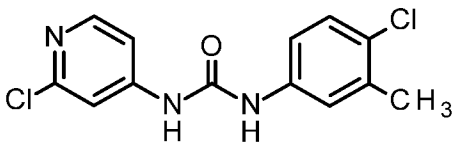
25 MS(ESI^{pos}): *m/z* = 283 (M+H)⁺.

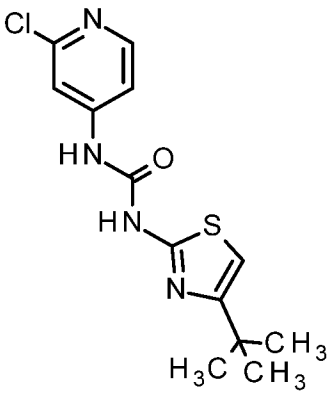
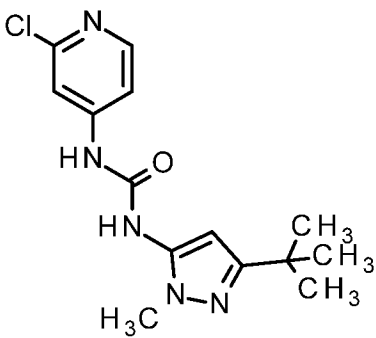
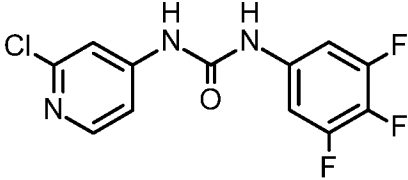
Example 22**1-(2-chloropyridin-4-yl)-3-(3-cyanophenyl)urea**

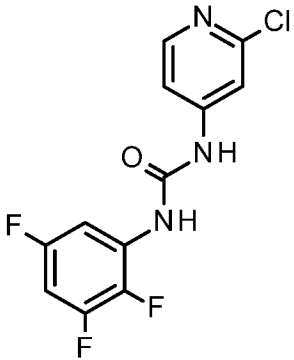
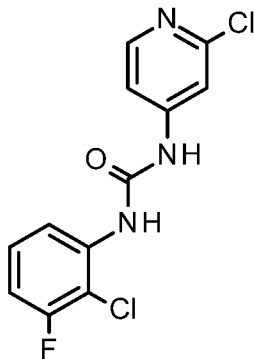
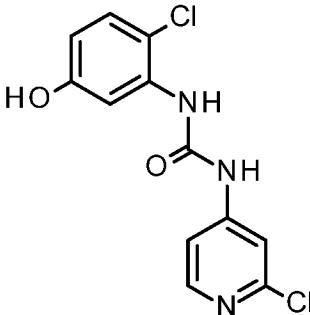
- 5 To intermediate **2** (45.6 mg, 150 μ mol) in 1mL NMP, 3-aminobenzonitrile (21.3 mg, 180 μ mol) in 0,27mL NMP and triethylamine (30.4 mg, 300 μ mol) in 1mL NMP were added. The reaction mixture was heated for 16h to 80°C. After cooling to room temperature, the reaction mixture was filtered through a pad of Alox N and purified by preparative HPLC (method D) to give 6.3 mg of the title compound.
- 10 **LC-MS (method 1): $R_t = 0.94$ min; MS (ESIpos): $m/z = 273$ $[M+H]^+$**

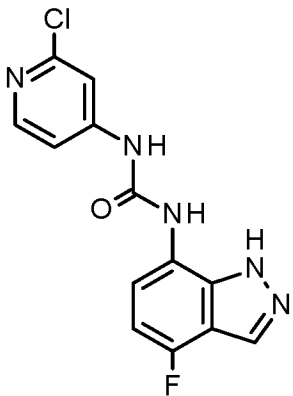
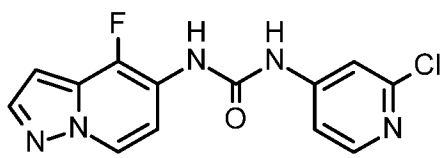
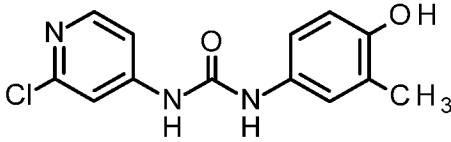
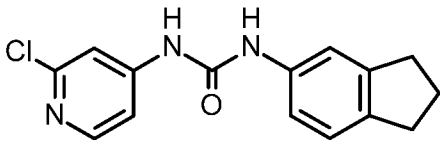
The examples in the following table were prepared in analogy to example **22**:

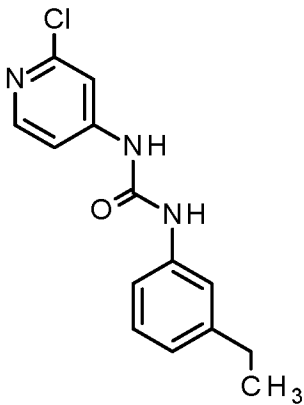
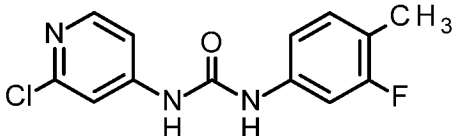
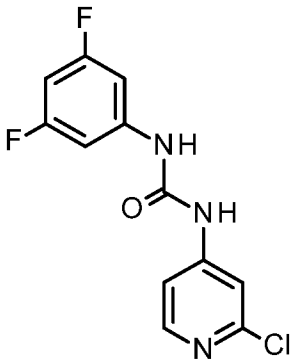
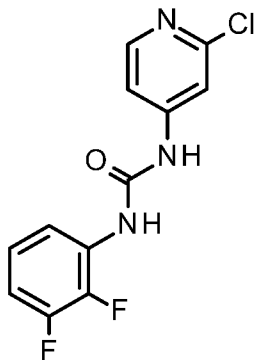
Example	Structure IUPAC-Name	LC-MS method 1 Retention time Mass found
23	 1-(2-chloropyridin-4-yl)-3-(4-methylphenyl)urea	$R_t = 0.89 \text{ min}$ $m/z = 262$ $[M+H]^+$
24	 1-(4-chlorophenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.07 \text{ min}$ $m/z = 282$ $[M+H]^+$
25	 1-(2-chloropyridin-4-yl)-3-(4-fluorophenyl)urea	$R_t = 0.91 \text{ min}$ $m/z = 266$ $[M+H]^+$
26	 1-(2-chloropyridin-4-yl)-3-isoquinolin-6-ylurea	$R_t = 0.86 \text{ min}$ $m/z = 299$ $[M+H]^+$

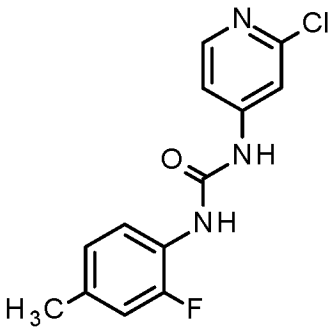
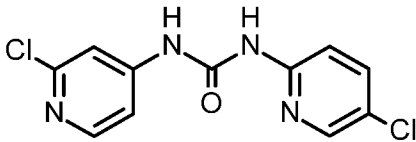
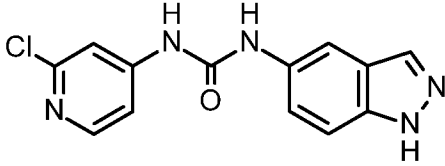
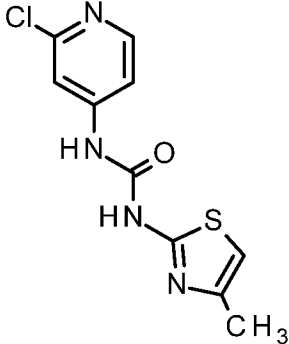
27	 1-(3-chloro-2-methylphenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.11 \text{ min}$ $m/z = 296$ $[M+H]^+$
28	 1-(2-chloro-4-methylphenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.15 \text{ min}$ $m/z = 296$ $[M+H]^+$
29	 1-(3-chloro-4-cyanophenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.07 \text{ min}$ $m/z = 307$ $[M+H]^+$
30	 1-(4-chloro-3-methylphenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.17 \text{ min}$ $m/z = 296$ $[M+H]^+$

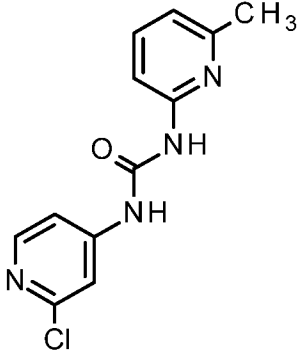
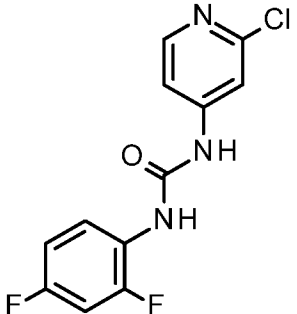
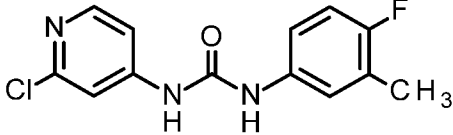
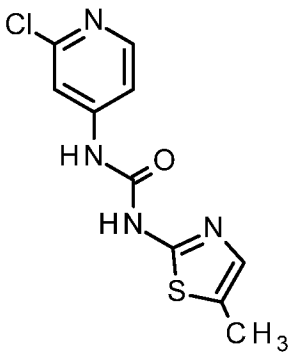
31	 1-(4-tert-butyl-1,3-thiazol-2-yl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.12 \text{ min}$ $m/z = 311$ $[M+H]^+$
32	 1-(3-tert-butyl-1-methyl-1H-pyrazol-5-yl)-3-(2-chloropyridin-4-yl)urea	$R_t = 0.98 \text{ min}$ $m/z = 308$ $[M+H]^+$
33	 1-(2-chloropyridin-4-yl)-3-(3,4,5-trifluorophenyl)urea	$R_t = 1.13 \text{ min}$ $m/z = 302$ $[M+H]^+$

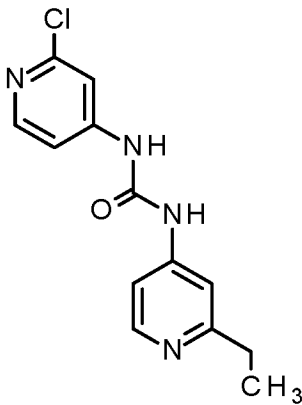
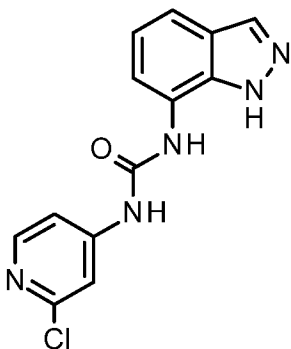
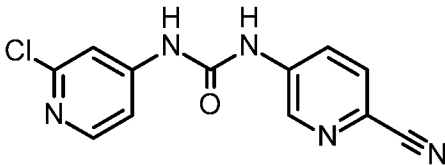
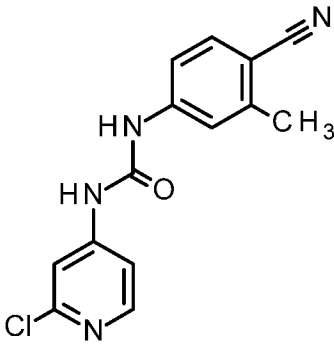
34	 1-(2-chloropyridin-4-yl)-3-(2,3,5-trifluorophenyl)urea	$R_t = 1.12 \text{ min}$ $m/z = 302$ $[M+H]^+$
35	 1-(2-chloro-3-fluorophenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.10 \text{ min}$ $m/z = 300$ $[M+H]^+$
36	 1-(2-chloro-5-hydroxyphenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 0.72 \text{ min}$ $m/z = 298$ $[M+H]^+$

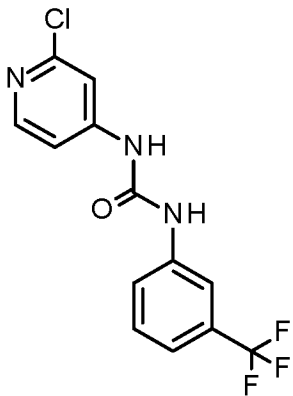
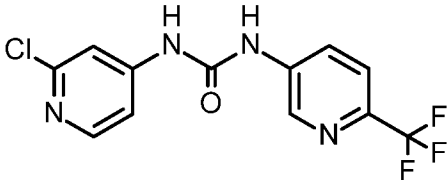
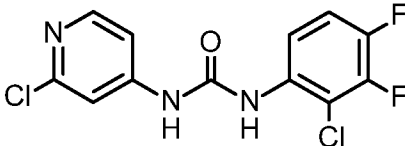
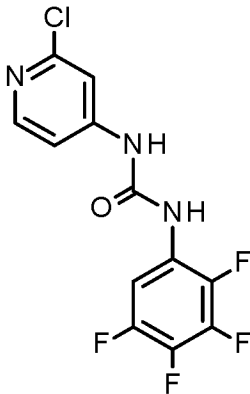
37	 1-(2-chloropyridin-4-yl)-3-(4-fluoro-1H-indazol-7-yl)urea	$R_t = 0.90 \text{ min}$ $m/z = 306$ $[M+H]^+$
38	 1-(2-chloropyridin-4-yl)-3-(4-fluoropyrazolo[1,5-a]pyridin-5-yl)urea	$R_t = 0.87 \text{ min}$ $m/z = 306$ $[M+H]^+$
39	 1-(2-chloropyridin-4-yl)-3-(4-hydroxy-3-methylphenyl)urea	$R_t = 0.77 \text{ min}$ $m/z = 278$ $[M+H]^+$
40	 1-(2-chloropyridin-4-yl)-3-(2,3-dihydro-1H-inden-5-yl)urea	$R_t = 1.16 \text{ min}$ $m/z = 288$ $[M+H]^+$

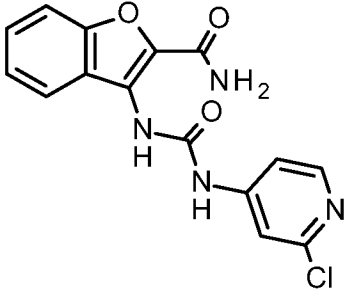
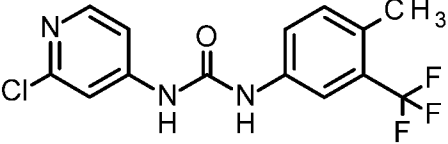
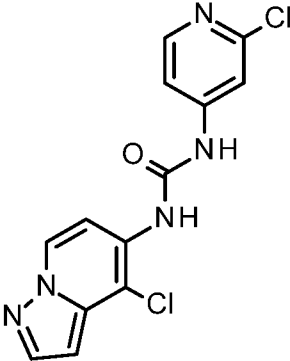
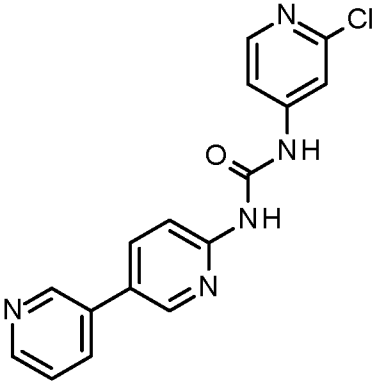
41	 1-(2-chloropyridin-4-yl)-3-(3-ethylphenyl)urea	$R_t = 1.14 \text{ min}$ $m/z = 276$ $[M+H]^+$
42	 1-(2-chloropyridin-4-yl)-3-(3-fluoro-4-methylphenyl)urea	$R_t = 1.11 \text{ min}$ $m/z = 280$ $[M+H]^+$
43	 1-(2-chloropyridin-4-yl)-3-(3,5-difluorophenyl)urea	$R_t = 1.11 \text{ min}$ $m/z = 284$ $[M+H]^+$
44	 1-(2-chloropyridin-4-yl)-3-(2,3-difluorophenyl)urea	$R_t = 1.06 \text{ min}$ $m/z = 284$ $[M+H]^+$

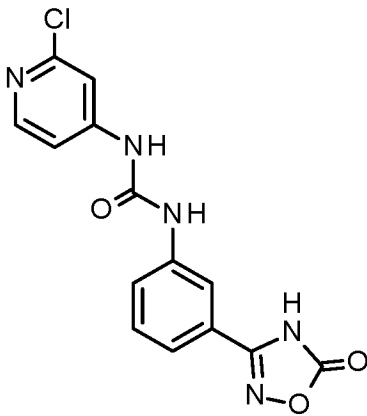
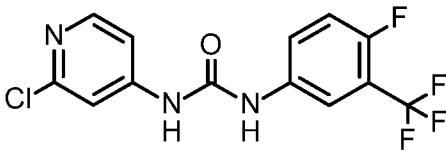
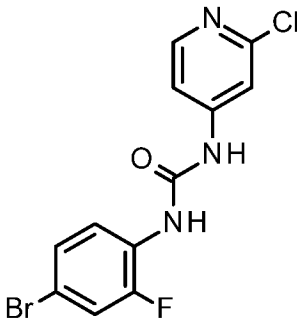
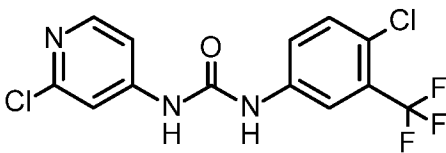
45	 1-(2-chloropyridin-4-yl)-3-(2-fluoro-4-methylphenyl)urea	$R_t = 1.09 \text{ min}$ $m/z = 280$ $[M+H]^+$
46	 1-(2-chloropyridin-4-yl)-3-(5-chloropyridin-2-yl)urea	$R_t = 1.07 \text{ min}$ $m/z = 283$ $[M+H]^+$
47	 1-(2-chloropyridin-4-yl)-3-(1H-indazol-5-yl)urea	$R_t = 0.75 \text{ min}$ $m/z = 288$ $[M+H]^+$
48	 1-(2-chloropyridin-4-yl)-3-(4-methyl-1,3-thiazol-2-yl)urea	$R_t = 0.72 \text{ min}$ $m/z = 269$ $[M+H]^+$

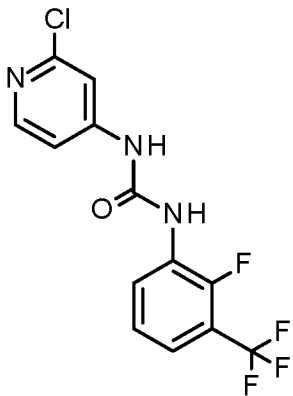
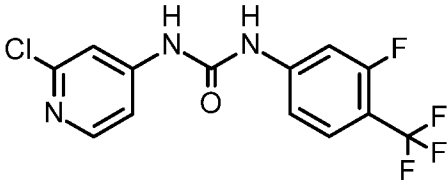
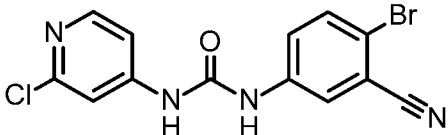
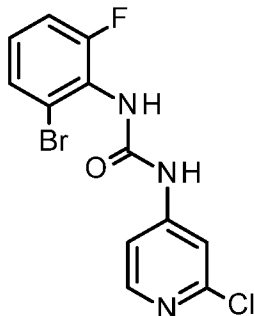
49	 1-(2-chloropyridin-4-yl)-3-(6-methylpyridin-2-yl)urea	$R_t = 1.02 \text{ min}$ $m/z = 263$ $[M+H]^+$
50	 1-(2-chloropyridin-4-yl)-3-(2,4-difluorophenyl)urea	$R_t = 1.03 \text{ min}$ $m/z = 284$ $[M+H]^+$
51	 1-(2-chloropyridin-4-yl)-3-(4-fluoro-3-methylphenyl)urea	$R_t = 1.08 \text{ min}$ $m/z = 280$ $[M+H]^+$
52	 1-(2-chloropyridin-4-yl)-3-(5-methyl-1,3-thiazol-2-yl)urea	$R_t = 0.74 \text{ min}$ $m/z = 269$ $[M+H]^+$

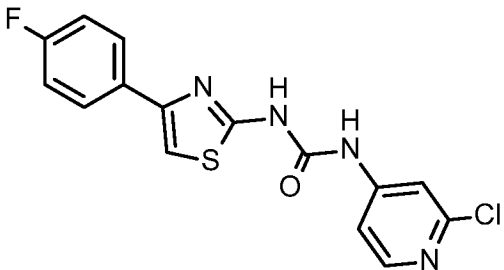
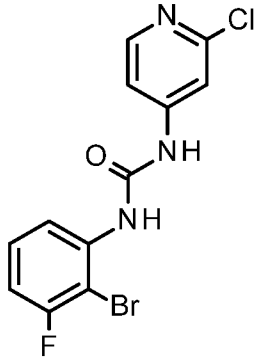
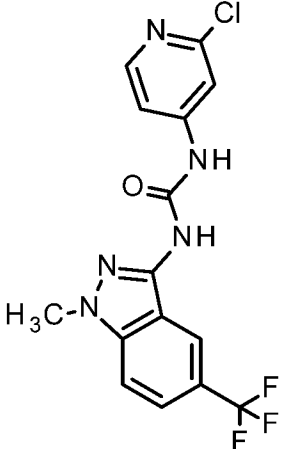
53	 1-(2-chloropyridin-4-yl)-3-(2-ethylpyridin-4-yl)urea	$R_t = 0.84 \text{ min}$ $m/z = 277$ $[M+H]^+$
54	 1-(2-chloropyridin-4-yl)-3-(1H-indazol-7-yl)urea	$R_t = 0.85 \text{ min}$ $m/z = 288$ $[M+H]^+$
55	 1-(2-chloropyridin-4-yl)-3-(6-cyanopyridin-3-yl)urea	$R_t = 0.85 \text{ min}$ $m/z = 274$ $[M+H]^+$
56	 1-(2-chloropyridin-4-yl)-3-(4-cyano-3-methylphenyl)urea	$R_t = 1.01 \text{ min}$ $m/z = 287$ $[M+H]^+$

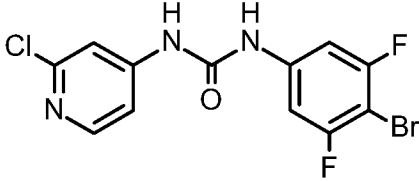
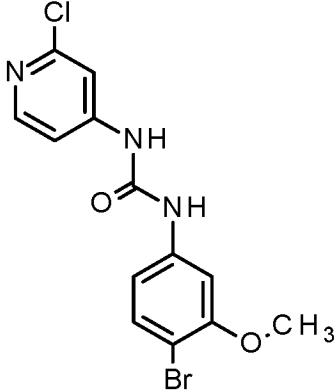
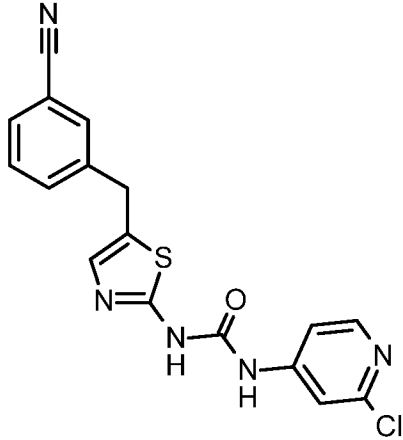
57	 1-(2-chloropyridin-4-yl)-3-[3-(trifluoromethyl)phenyl]urea	$R_t = 1.16 \text{ min}$ $m/z = 316$ $[M+H]^+$
58	 1-(2-chloropyridin-4-yl)-3-[6-(trifluoromethyl)pyridin-3-yl]urea	$R_t = 1.03 \text{ min}$ $m/z = 317$ $[M+H]^+$
59	 1-(2-chloro-3,4-difluorophenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.13 \text{ min}$ $m/z = 318$ $[M+H]^+$
60	 1-(2-chloropyridin-4-yl)-3-(2,3,4,5-tetrafluorophenyl)urea	$R_t = 1.18 \text{ min}$ $m/z = 320$ $[M+H]^+$

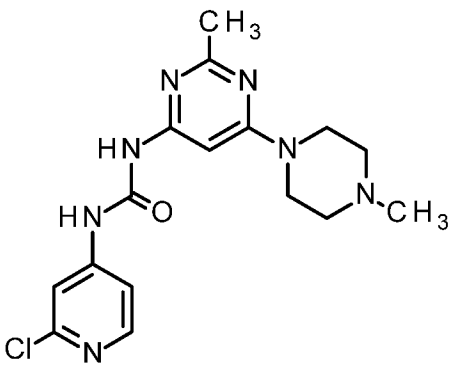
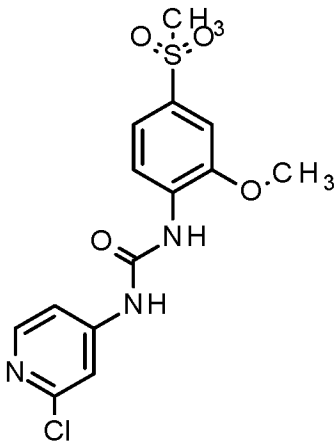
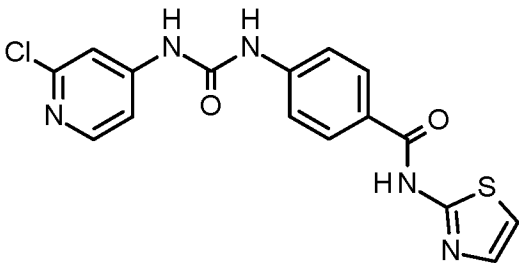
61	 3-[[2-chloropyridin-4-yl]carbamoyl]amino-1-benzofuran-2-carboxamide	$R_t = 0.99 \text{ min}$ $m/z = 331$ $[M+H]^+$
62	 1-(2-chloropyridin-4-yl)-3-[4-methyl-3-(trifluoromethyl)phenyl]urea	$R_t = 1.23 \text{ min}$ $m/z = 330$ $[M+H]^+$
63	 1-(4-chloropyrazolo[1,5-a]pyridin-5-yl)-3-(2-chloropyridin-4-yl)urea	$R_t = 0.96 \text{ min}$ $m/z = 322$ $[M+H]^+$
64	 1-[3,3'-bipyridin]-6-yl-3-(2-chloropyridin-4-yl)urea	$R_t = 0.93 \text{ min}$ $m/z = 326$ $[M+H]^+$

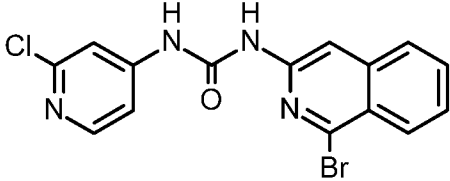
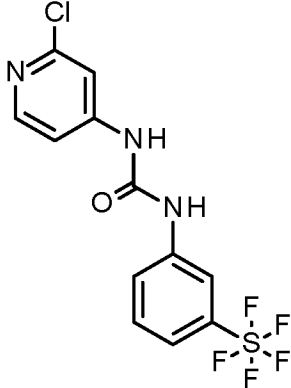
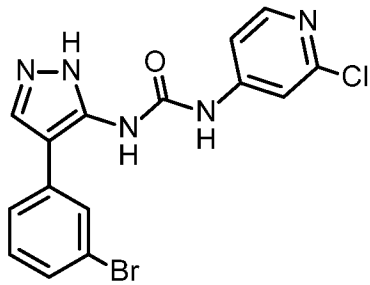
65	 1-(2-chloropyridin-4-yl)-3-[3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)phenyl]urea	$R_t = 0.93 \text{ min}$ $m/z = 332$ $[M+H]^+$
66	 1-(2-chloropyridin-4-yl)-3-[4-fluoro-3-(trifluoromethyl)phenyl]urea	$R_t = 1.19 \text{ min}$ $m/z = 334$ $[M+H]^+$
67	 1-(4-bromo-2-fluorophenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.18 \text{ min}$ $m/z = 346$ $[M+H]^+$
68	 1-(2-chloropyridin-4-yl)-3-[4-chloro-3-(trifluoromethyl)phenyl]urea	$R_t = 1.27 \text{ min}$ $m/z = 350$ $[M+H]^+$

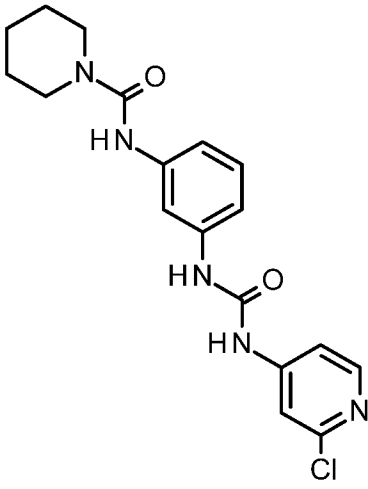
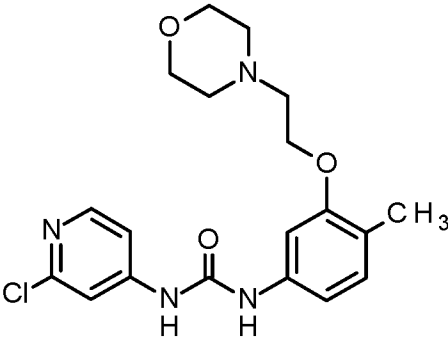
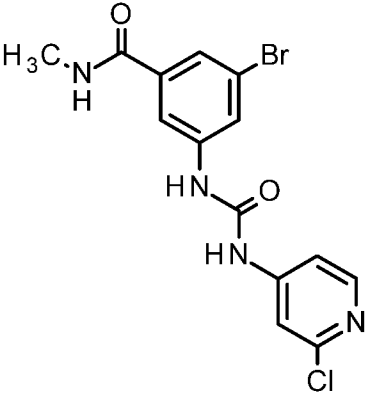
69	 1-(2-chloropyridin-4-yl)-3-[2-fluoro-3-(trifluoromethyl)phenyl]urea	$R_t = 1.20 \text{ min}$ $m/z = 334$ $[M+H]^+$
70	 1-(2-chloropyridin-4-yl)-3-[3-fluoro-4-(trifluoromethyl)phenyl]urea	$R_t = 1.23 \text{ min}$ $m/z = 334$ $[M+H]^+$
71	 1-(4-bromo-3-cyanophenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.10 \text{ min}$ $m/z = 353$ $[M+H]^+$
72	 1-(2-bromo-6-fluorophenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 0.97 \text{ min}$ $m/z = 346$ $[M+H]^+$

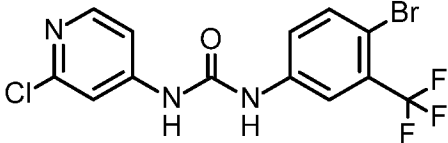
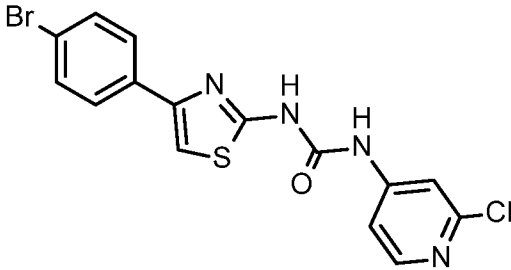
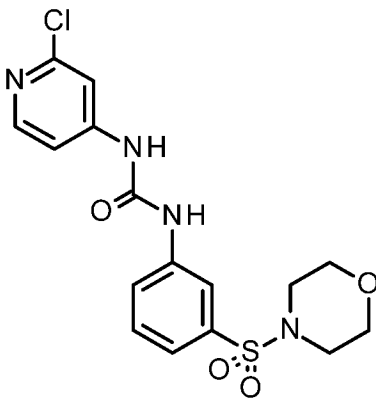
73	 1-(2-chloropyridin-4-yl)-3-[4-(4-fluorophenyl)-1,3-thiazol-2-yl]urea	$R_t = 0.92 \text{ min}$ $m/z = 349$ $[M+H]^+$
74	 1-(2-bromo-3-fluorophenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.11 \text{ min}$ $m/z = 346$ $[M+H]^+$
75	 1-(2-chloropyridin-4-yl)-3-[1-methyl-5-(trifluoromethyl)-1H-indazol-3-yl]urea	$R_t = 1.16 \text{ min}$ $m/z = 370$ $[M+H]^+$

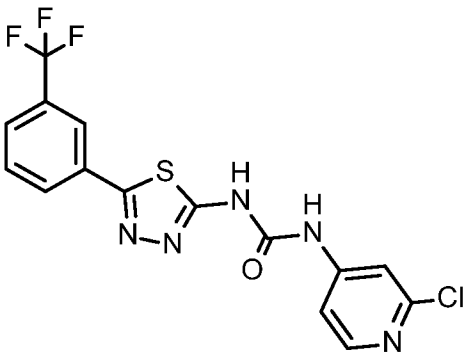
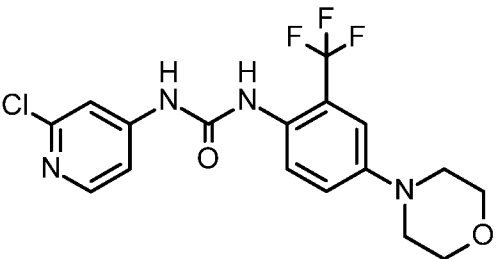
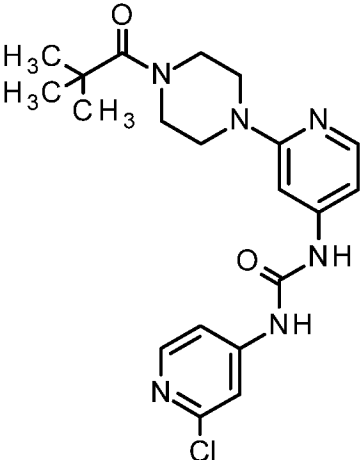
76	 1-(4-bromo-3,5-difluorophenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.24 \text{ min}$ $m/z = 364$ $[M+H]^+$
77	 1-(4-bromo-3-methoxyphenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.12 \text{ min}$ $m/z = 358$ $[M+H]^+$
78	 1-(2-chloropyridin-4-yl)-3-[5-(3-cyanobenzyl)-1,3-thiazol-2-yl]urea	$R_t = 0.87 \text{ min}$ $m/z = 370$ $[M+H]^+$

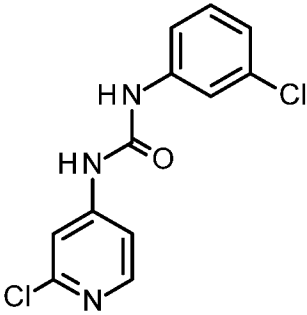
79	 1-(2-chloropyridin-4-yl)-3-[2-methyl-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl]urea	$R_t = 1.01 \text{ min}$ $m/z = 362$ $[M+H]^+$
80	 1-(2-chloropyridin-4-yl)-3-[2-methoxy-4-(methylsulfonyl)phenyl]urea	$R_t = 0.91 \text{ min}$ $m/z = 356$ $[M+H]^+$
81	 4-([(2-chloropyridin-4-yl)carbamoyl]amino)-N-(1,3-thiazol-2-yl)benzamide	$R_t = 0.82 \text{ min}$ $m/z = 374$ $[M+H]^+$

82	 1-(1-bromoisoquinolin-3-yl)-3-(2-chloropyridin-4-yl)urea	$R_t = 1.26 \text{ min}$ $m/z = 379$ $[M+H]^+$
83	 1-(2-chloropyridin-4-yl)-3-[3-(pentafluoro-lambda⁶-sulfanyl)phenyl]urea	$R_t = 1.21 \text{ min}$ $m/z = 374$ $[M+H]^+$
84	 1-[4-(3-bromophenyl)-1H-pyrazol-5-yl]-3-(2-chloropyridin-4-yl)urea	$R_t = 0.96 \text{ min}$ $m/z = 394$ $[M+H]^+$

85	 N-(3-([(2-chloropyridin-4-yl)carbamoyl]amino}phenyl)piperidine-1-carboxamide	$R_t = 0.97 \text{ min}$ $m/z = 374$ $[M+H]^+$
86	 1-(2-chloropyridin-4-yl)-3-{4-methyl-3-[2-(morpholin-4-yl)ethoxy]phenyl}urea	$R_t = 1.02 \text{ min}$ $m/z = 391$ $[M+H]^+$
87	 3-bromo-5-([(2-chloropyridin-4-yl)carbamoyl]amino}-N-methylbenzamide	$R_t = 0.92 \text{ min}$ $m/z = 385$ $[M+H]^+$

88	 1-[4-bromo-3-(trifluoromethyl)phenyl]-3-(2-chloropyridin-4-yl)urea	$R_t = 1.25 \text{ min}$ $m/z = 396$ $[M+H]^+$
89	 1-[4-(4-bromophenyl)-1,3-thiazol-2-yl]-3-(2-chloropyridin-4-yl)urea	$R_t = 1.02 \text{ min}$ $m/z = 411$ $[M+H]^+$
90	 1-(2-chloropyridin-4-yl)-3-[3-(morpholin-4-ylsulfonyl)phenyl]urea	$R_t = 0.92 \text{ min}$ $m/z = 397$ $[M+H]^+$

91	 1-(2-chloropyridin-4-yl)-3-{5-[3-(trifluoromethyl)phenyl]-1,3,4-thiadiazol-2-yl}urea	$R_t = 0.69 \text{ min}$ $m/z = 400$ $[M+H]^+$
92	 1-(2-chloropyridin-4-yl)-3-[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]urea	$R_t = 1.01 \text{ min}$ $m/z = 401$ $[M+H]^+$
93	 1-(2-chloropyridin-4-yl)-3-{2-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]pyridin-4-yl}urea	$R_t = 1.00 \text{ min}$ $m/z = 417$ $[M+H]^+$

94	 1-(3-chlorophenyl)-3-(2-chloropyridin-4-yl)urea	$R_t = 0.87 \text{ min}$ $m/z = 281$ $[M+H]^+$
----	--	--

EXPERIMENTAL SECTION – BIOLOGICAL ASSAYS

Examples were tested in selected biological assays one or more times. When tested more than once, data are reported as either average values or as median values, wherein

- the average value, also referred to as the arithmetic mean value, represents the sum of the values obtained divided by the number of times tested, and
- the median value represents the middle number of the group of values when ranked in ascending or descending order. If the number of values in the data set is odd, the median is the middle value. If the number of values in the data set is even, the median is the arithmetic mean of the two middle values.

Examples were synthesized one or more times. When synthesized more than once, data from biological assays represent average values or median values calculated utilizing data sets obtained from testing of one or more synthetic batch.

- The *in vitro* activity of the compounds of the present invention can be demonstrated in the following assays:

***In vitro* assay 1: SMARCA2 ATPase assay**

For characterization of ATPase inhibitors of SMARCA2, a SWI/SNF minimal complex (Phelan et. al, Molecular Cell, 3, 247-253, 1999) consisting of full length SMARCA2 with C-terminal FLAG tag and SWI/SNF subunits BAF47, BAF155 and BAF170 was recombinantly expressed in Hi5 cells and purified using affinity chromatography and size exclusion chromatography.

A SMARCA2 ADP Kinase Assay (Promega, #V9101) was used to characterize inhibitors of SMARCA2 activity via luminescent endpoint determination. The enzymatic turnover of ATP to ADP was monitored by a coupled, ATP dependent, luminescent luciferase reaction. SMARCA2 activity was determined by quantifying residual ATP content after 30 min of enzymatic reaction. Compounds that inhibit SMARCA2 were detected by detecting a decrease in luminescent signal in comparison to control reaction without test compound. IC₅₀ values of the test compounds was determined by plotting the compound concentration vs the percentage of SMARCA2 activity by interpolation. % remaining activity values of the test compounds are determined by measuring ATPase activity at 12.5 μ M final compound concentration. A remaining activity (relative to DMSO control) of >50% is regarded as inactive compound, a remaining activity of <50% is regarded as active compound. The results of this analysis are shown at Table 1 (below).

Detailed Assay description: Compounds of interest (dissolved in DMSO; concentration 10 nM-100 μ M, 1 μ L/well) were added to a 384-MTP plate (Greiner, #781075). Next, 30 μ L/well SMARCA2 was added (Complex: SMARCA2 + BAF47 + BAF155 + BAF170; 184641 kDa; final concentration 2.75 μ g/ml). The enzyme reaction was started by addition of 20 μ L pUC19 plasmid (BAYOU Biolabs, LLC., #P-102; final concentration 1.88 nM) plus ATP (Ultra Pure ATP, Promega, #V915B; final concentration 0.4 mM). All components were dissolved in reaction buffer (20 mM Hepes, pH 7.9, 0.5 mM EDTA, 100 mM KCL, 2.0 mM MgCL₂, 0.6 mM Glutathione, 0.01% BSA, 0.02% Tween 80). Total test volume was 51 μ L. The reaction was incubated for 30 min time at 37°C (SMARCA2 dark reaction). Afterwards ADP Glo Reagent (20 μ L) was added and incubated for 25 min at 30°C. At last Kinase Detection Buffer (20 μ L) was added and incubated for 60 min at 30°C. The reaction was monitored by luminescent measurement via BMG ClarioStar.

Table 1: SMARCA2 ATPase : IC₅₀ / %Remaining values of examples in *in vitro* assay 1

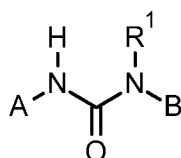
Example	SMARCA2 IC ₅₀ [M]	ATPase %Remaining [%]
1	7,40 E-7	
2	2,00 E-6	
3	6,60 E-6	
4	4,30 E-6	
5	2,10 E-6	
6	6,50 E-6	
7	2,40 E-6	
8	5,70 E-7	
9	3,20 E-6	
10	9,90 E-7	
11	4,70 E-6	
12	9,20 E-6	
13	2,60 E-6	
14	8,20 E-7	
15	1,10 E-6	
16	4,00 E-6	
17	3,89 E-7	
18	5,50 E-6	
19	1,10 E-6	
20	3,10 E-6	
21	8,50 E-6	
22		43,00
23		49,00
24		34,00
25		49,00
26		31,00
27	1,70 E-6	
28	5,20 E-6	
29	1,80 E-6	
30	2,30 E-6	
31	2,90 E-6	
32	1,70 E-6	
33	6,60 E-6	

34	8,80 E-6	
35	6,00 E-6	
36	2,10 E-6	
37	3,40 E-6	
38	3,60 E-6	
39	6,20 E-6	
40		43,00
41		49,00
42	3,30 E-6	
43	4,90 E-6	
44	1,80 E-6	
45	4,00 E-6	
46	3,40 E-6	
47		41,00
48	2,30 E-6	
49	3,80 E-6	
50		46,00
51		45,00
52		45,00
53	1,10 E-6	
54	3,30 E-6	
55	2,80 E-7	
56	2,60 E-6	
57	3,80 E-6	
58	2,80 E-6	
59	2,70 E-6	
60		41,00
61	1,70 E-6	
62		48,00
63	2,10 E-6	
64	1,95 E-6	
65	6,20 E-7	
66		44,00
67	2,75 E-6	
68		45,00

69		46,00
70		50,00
71	2,90 E-6	
72	4,10 E-6	
73	1,60 E-6	
74	4,15 E-6	
75		42,00
76	2,30 E-6	
77	2,25 E-6	
78	2,20 E-6	
79	2,65 E-6	
80		48,00
81	2,90 E-6	
82		44,00
83		47,00
84		45,00
85	4,15 E-6	
86		46,00
87	2,40 E-6	
88	3,90 E-6	
89	8,95 E-7	
90		41,00
91	3,35 E-6	
92	3,75 E-6	
93	1,95 E-6	
94	4,10 E-6	

CLAIMS

1. A compound of general formula (I):



(I),

5 in which

A is a pyridinyl group which is optionally substituted by R² and/or R³;

R¹ is a hydrogen atom or a methyl group;

R² is a halogen atom;

R³ is a hydrogen atom, a halogen atom or a C₁-C₃-alkyl group;

10 B a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom,

a C₁-C₃-alkyl group,

a C₁-C₃-haloalkyl group,

15 a C₁-C₃-alkoxy group,

a cyano group,

a hydroxy group,

a SF₅ group,

a -S(O)₂-(C₁-C₃-alkyl) group,

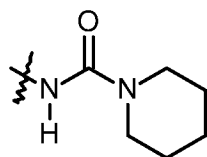
20 a N(O)₂ group,

a heteroaryl group,

a heterocycloalkyl group,

a -O-(C₁-C₃-alkyl)-heterocycloalkyl,

a -S(O)₂-heterocycloalkyl group,



25 a group and

a C(O)NR⁴R⁵, wherein

R⁴ is a hydrogen atom or a C₁-C₃-alkyl group;

R⁵ is a hydrogen atom, a C₁-C₃-alkyl group, or a heteroaryl group;
a pyridinyl group,
which is optionally substituted with one or more substituents and each
substituent is independently selected from
5 a halogen atom,
a cyano group,
a C₁-C₃-alkyl group,
a C₁-C₃-haloalkyl group,
a C₁-C₃-alkoxy group,
10 a C₃-C₆-cycloalkyl group,
a phenyl group, which is optionally substituted with a halogen atom, a C₁-
C₃-alkyl group, C₁-C₃-alkoxy group, a CN group, a NR⁴R⁵ group;
a heteroaryl group and
a piperazinyl group, which is optionally substituted with a C(O)R⁶ group,
15 wherein
R⁶ is a C₁-C₄-alkyl group,;
a pyrimidinyl group,
which is optionally substituted with a C₁-C₃-alkyl group, or
a piperazinyl group,
20 which is optionally further substituted with a C₁-C₃-alkyl group;
a thiazolyl group, which is optionally substituted one or two times and each
substituent is independently selected from
a C₁-C₄-alkyl group,
a phenyl group which itself is optionally further substituted with a halogen
25 atom or a C₁-C₃-haloalkyl group, and
a -CH₂-phenyl group which itself is optionally further substituted with a
cyano group;
a pyrazolyl group, which is optionally substituted one or more times with a C₁-C₄-
alkyl group or a phenyl group which itself is optionally substituted with a
30 halogen atom,
a thiadiazolyl group which is optionally substituted with a phenyl group which itself
is optionally further substituted with a C₁-C₃-haloalkyl group, or a phenyl
group which itself is optionally further substituted with a halogen atom or a
C₁-C₃-haloalkyl group;

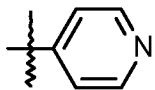
- a benzofuranyl group, which is optionally substituted with a $C(O)NR^4R^5$ group,
 a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen atom;
 an indazolyl group which is optionally substituted one or more substituents and
 5 each substituent independently selected from a halogen atom, a C_1 - C_3 -alkyl group, a C_1 - C_3 -haloalkyl group,
 an isoquinolinyl group which is optionally substituted with a halogen atom, and
 an dihydroindenyl group;

with the proviso that

- 10 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
 15 1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

- 20 2. The compound according to claim 1, wherein:

A is a  group which is optionally substituted by R^2 and/or R^3 ;

R^1 is a hydrogen atom;

R^2 is a halogen atom;

R^3 is a hydrogen atom or a halogen atom;

- 25 B a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from
 a halogen atom,
 a C_1 - C_3 -alkyl group,
 a C_1 - C_3 -haloalkyl group,
 30 a C_1 - C_3 -alkoxy group,
 a cyano group,

a hydroxy group,
a heteroaryl group,
a heterocycloalkyl group,
a C(O)NR⁴R⁵, wherein

5 R⁴ is a hydrogen atom or a C₁-C₃-alkyl group;

R⁵ is a hydrogen atom, a C₁-C₃-alkyl group, a heteroaryl group or
a -(C₁-C₃-alkyl)-O-heteroaryl group;

a pyridinyl group,

10 which is optionally substituted with one or more substituents and each
substituent is independently selected from

a halogen atom,

a cyano group,

a C₁-C₃-alkyl group,

a C₁-C₃-haloalkyl group,

15 a C₁-C₃-alkoxy group,

a phenyl group, a heteroaryl group, and

a piperazinyl group, which is optionally substituted with a C(O)R⁶ group,
wherein

R⁶ is a C₁-C₄-alkyl group;

20 a pyrimidinyl group which is optionally substituted with a C₁-C₃-alkyl group, or a
piperazinyl group which itself is optionally further substituted with a C₁-C₃-
alkyl group;

a thiazol-2-yl group, which is optionally substituted one or two times and each
substituent is independently selected from

25 a C₁-C₄-alkyl group,

a phenyl group which itself is optionally further substituted with a halogen
atom or a C₁-C₃-haloalkyl group, and

a -CH₂-phenyl group which itself is optionally further substituted with a
cyano group;

30 a pyrazol-5-yl group, which is optionally substituted one or more times with a C₁-
C₄-alkyl group or a phenyl group which itself is optionally substituted with
a halogen atom;

a benzofuran-3-yl group, which is optionally substituted with a C(O)NR⁴R⁵ group;

a pyrazolo[1,5-a]pyridinyl group which is optionally substituted with a halogen atom;

an indazol-7-yl group which is optionally substituted one or more substituents and each substituent independently selected from a halogen atom, a C₁-C₃-alkyl group, a C₁-C₃-haloalkyl group;

with the proviso that

1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,

1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,

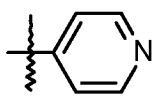
10 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and

1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

or a stereoisomer, a tautomer, a hydrate, a solvate, or a salt thereof, or a salt of a stereoisomer, or a salt of a tautomer, or a salt of a hydrate, or a salt of a solvate, or a mixture of same.

3. The compound according to claim 1 or 2, wherein:

A is a  group which is optionally substituted by R² and/or R³, or

R¹ is a hydrogen atom,

20 R² is a halogen atom,

R³ is a hydrogen atom,

B a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom

25 a C₁-C₃-alkyl group,

a C₁-C₃-haloalkyl group,

a C₁-C₃-alkoxy group,

a cyano group,

a heteroaryl group,

30 is a pyridinyl group,

which is optionally substituted with one or more substituents and each substituent is independently selected from

- 5 a halogen atom,
a cyano group,
a C₁-C₃-alkyl group,
a C₁-C₃-haloalkyl group,
a C₁-C₃-alkoxy group,
a phenyl group, and
a piperazinyl group, which is optionally substituted with a C(O)R⁶ group,
a thiazol-2-yl group, which is optionally substituted one or two times and each
substituent is independently selected from
10 a C₁-C₄-alkyl group,
a phenyl group which itself is optionally further substituted with a halogen
atom or a C₁-C₃-haloalkyl group, and
a -CH₂-phenyl group which itself is optionally further substituted with a cyano
group;
15 a pyrazol-5-yl group, which is optionally substituted one or more times with a C₁-
C₄-alkyl group or a phenyl group which itself is optionally substituted with a
halogen atom,
a benzofuran-3-yl group, which is optionally substituted with a C(O)NR⁴R⁵ group,
a pyrazolo[1,5-a]pyridin group which is optionally substituted with a halogen atom;
20 an indazol-7-yl group which is optionally substituted one or more substituents and
each substituent independently selected from a halogen atom, a C₁-C₃-alkyl
group, a C₁-C₃-haloalkyl group;

R⁴ is a hydrogen atom or a C₁-C₃-alkyl group;

R⁵ is a hydrogen atom or a C₁-C₃-alkyl group; and

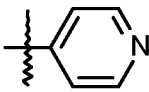
- 25 R⁶ is a C₁-C₄-alkyl group, or a pyridinyl group;

with the proviso that

- 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
30 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

or a stereoisomer, a tautomer, an N-oxide, a hydrate, a solvate, or a salt, a salt of a stereoisomer, a salt of a tautomer, a salt of an N-oxide, a salt of a hydrate, a salt of a solvate, or a mixture of same.

5 4. The compound according to claim 1, 2 or 3, wherein:

A is a  group which is optionally substituted by R² and/or R³, or

R¹ is a hydrogen atom,

R² is a halogen atom,

R³ is a hydrogen atom,

10 B a phenyl group, which is optionally substituted with one or more substituents and each substituent is independently selected from

a halogen atom,

a C₁-C₃-alkyl group,

a C₁-C₃-haloalkyl group,

15 a C₁-C₃-alkoxy group,

a cyano group,

a heteroaryl group

is a pyridinyl group,

which is optionally substituted with one or more substituents and each substituent is independently selected from

20 a halogen atom,

a cyano group,

a C₁-C₃-alkyl group,

a C₁-C₃-haloalkyl group,

25 a C₁-C₃-alkoxy group,

a phenyl group, and

a piperidinyl group, which is optionally substituted with a C(O)R⁶ group, and

R⁶ is a C₁-C₄-alkyl group, or a pyridinyl group,

with the proviso that

30 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,

1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,

1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

5 or a stereoisomer, a tautomer, an N-oxide, a hydrate, a solvate, or a salt, a salt of a stereoisomer, a salt of a tautomer, a salt of an N-oxide, a salt of a hydrate, a salt of a solvate, or a mixture of same.

5. The compound according to claim 1 which is selected from the group:

1-(2-fluoropyridin-4-yl)-3-[2-(trifluoromethyl)pyridin-4-yl]urea
1-(2-chloro-6-methylpyridin-4-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[2-chloro-6-(trifluoromethyl)pyridin-4-yl]urea,
1-(2-chloropyridin-4-yl)-3-[4-hydroxy-3-(trifluoromethyl)phenyl]urea,
1-(3-chloro-4-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloro-6-methoxypyridin-4-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3,4-dichlorophenyl)urea,
1,3-bis(2,6-dichloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2,6-dichloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-phenylpyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(6-chloropyridin-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3-cyano-4-fluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(6-chloropyridin-3-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-fluoropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-cyclopropylpyridin-4-yl)urea,
1,3-bis(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2-methoxypyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3-cyanophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(4-methylphenyl)urea,
1-(4-chlorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluorophenyl)urea,

1-(2-chloropyridin-4-yl)-3-isoquinolin-6-ylurea,
1-(3-chloro-2-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloro-4-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(3-chloro-4-cyanophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-chloro-3-methylphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-tert-butyl-1,3-thiazol-2-yl)-3-(2-chloropyridin-4-yl)urea,
1-(3-tert-butyl-1-methyl-1H-pyrazol-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3,4,5-trifluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3,5-trifluorophenyl)urea,
1-(2-chloro-3-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloro-5-hydroxyphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoro-1H-indazol-7-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoropyrazolo[1,5-a]pyridin-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-hydroxy-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3-dihydro-1H-inden-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(3-ethylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3-fluoro-4-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(3,5-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2,3-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2-fluoro-4-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(5-chloropyridin-2-yl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-5-yl)urea,
1-(2-chloropyridin-4-yl)-3-(2,4-difluorophenyl)urea,
1-(2-chloropyridin-4-yl)-3-(4-fluoro-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-(2-ethylpyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-(1H-indazol-7-yl)urea,
1-(2-chloropyridin-4-yl)-3-(6-cyanopyridin-3-yl)urea,
1-(2-chloropyridin-4-yl)-3-(4-cyano-3-methylphenyl)urea,
1-(2-chloropyridin-4-yl)-3-[3-(trifluoromethyl)phenyl]urea,
1-(2-chloro-3,4-difluorophenyl)-3-(2-chloropyridin-4-yl)urea,

1-(2-chloropyridin-4-yl)-3-(2,3,4,5-tetrafluorophenyl)urea,
3-[[2-(2-chloropyridin-4-yl)carbamoyl]amino]-1-benzofuran-2-carboxamide,
1-(2-chloropyridin-4-yl)-3-[4-methyl-3-(trifluoromethyl)phenyl]urea,
1-(4-chloropyrazolo[1,5-a]pyridin-5-yl)-3-(2-chloropyridin-4-yl)urea,
1-[3,3'-bipyridin]-6-yl-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[4-fluoro-3-(trifluoromethyl)phenyl]urea,
1-(4-bromo-2-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[4-chloro-3-(trifluoromethyl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[2-fluoro-3-(trifluoromethyl)phenyl]urea,
1-(2-chloropyridin-4-yl)-3-[3-fluoro-4-(trifluoromethyl)phenyl]urea,
1-(4-bromo-3-cyanophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-bromo-6-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[4-(4-fluorophenyl)-1,3-thiazol-2-yl]urea,
1-(2-bromo-3-fluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[1-methyl-5-(trifluoromethyl)-1H-indazol-3-yl]urea,
1-(4-bromo-3,5-difluorophenyl)-3-(2-chloropyridin-4-yl)urea,
1-(4-bromo-3-methoxyphenyl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[5-(3-cyanobenzyl)-1,3-thiazol-2-yl]urea,
1-(2-chloropyridin-4-yl)-3-[2-methyl-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl]urea,
1-(2-chloropyridin-4-yl)-3-[2-methoxy-4-(methylsulfonyl)phenyl]urea,
4-[[2-(2-chloropyridin-4-yl)carbamoyl]amino]-N-(1,3-thiazol-2-yl)benzamide,
1-(1-bromoisoquinolin-3-yl)-3-(2-chloropyridin-4-yl)urea,
1-(2-chloropyridin-4-yl)-3-[3-(pentafluoro-lambda⁶-sulfanyl)phenyl]urea,
1-[4-(3-bromophenyl)-1H-pyrazol-5-yl]-3-(2-chloropyridin-4-yl)urea,
N-(3-[[2-(2-chloropyridin-4-yl)carbamoyl]amino]phenyl)piperidine-1-carboxamide,
1-(2-chloropyridin-4-yl)-3-{4-methyl-3-[2-(morpholin-4-yl)ethoxy]phenyl}urea,
3-bromo-5-[[2-(2-chloropyridin-4-yl)carbamoyl]amino]-N-methylbenzamide,
1-[4-bromo-3-(trifluoromethyl)phenyl]-3-(2-chloropyridin-4-yl)urea,
1-[4-(4-bromophenyl)-1,3-thiazol-2-yl]-3-(2-chloropyridin-4-yl)urea,

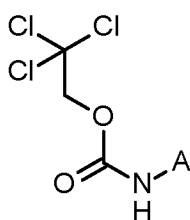
1-(2-chloropyridin-4-yl)-3-[3-(morpholin-4-ylsulfonyl)phenyl]urea,
 1-(2-chloropyridin-4-yl)-3-{5-[3-(trifluoromethyl)phenyl]-1,3,4-thiadiazol-2-yl}urea,
 1-(2-chloropyridin-4-yl)-3-[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]urea,
 1-(2-chloropyridin-4-yl)-3-{2-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]pyridin-4-yl}urea and
 1-(3-chlorophenyl)-3-(2-chloropyridin-4-yl)urea

with the proviso that

- 1-(2-chloropyridin-4-yl)-3-(pyridin-2-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(pyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(4-methylthiazol-2-yl)urea,
 5 1-(2-chloropyridin-4-yl)-3-(2-methylpyridin-4-yl)urea,
 1-(2-chloropyridin-4-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea and
 1-(2-chloropyridin-4-yl)-3-(2-(difluoromethyl)pyridin-4-yl)urea are excluded;

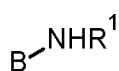
or a stereoisomer, a tautomer, an N-oxide, a hydrate, a solvate, or a salt, a salt of a stereoisomer, a salt of a tautomer, a salt of an N-oxide, a salt of a hydrate, a salt of a solvate, or a mixture of same.

6. A method of preparing a compound of general formula (I) according to any one of claims 1 to 5, said method comprising the step of allowing an intermediate compound of general formula (II) :



(II),

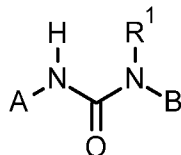
in which A is as defined for the compound of general formula (I) as defined *supra*,
 to react with a compound of general formula (III) :



(III),

in which B is as defined for the compound of general formula (I) as defined *supra*,

thereby giving a compound of general formula (I) :



(I),

in which R¹, A and B are as defined *supra*.

- 5 then optionally converting said compound into solvates, salts and/or solvates of such salts using the corresponding (i) solvents and/or (ii) bases or acids.

7. A compound of general formula (I) according to any one of claims 1 to 5 for use in the treatment or prophylaxis of a disease.

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8. A pharmaceutical composition comprising a compound of general formula (I) according to any one of claims 1 to 5 and one or more pharmaceutically acceptable excipients.

9. A pharmaceutical combination comprising:

- 15 • one or more first active ingredients, in particular compounds of general formula (I) according to any one of claims 1 to 5, and
- one or more further active ingredients, in particular anti-cancer agents.

10. A method of using a compound of general formula (I) according to any one of claims 1 to 5 for the treatment or prophylaxis of a disease.

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11. Use of a compound of general formula (I) according to any one of claims 1 to 5 for the preparation of a medicament for the treatment or prophylaxis of a disease.

25 12. Use according to claim 7, 10 or 11, wherein the disease is a hyperproliferative disorder, such as a cancer disorder.

13. A method for the treatment or prophylaxis of a disease comprising the administration of a compound according to any one of claims 1 to 5.

14. The method according to claim 13, wherein said disease is cancer.