nonspecific.

Current treatments for NLRP3-related diseases include biologic agents that target IL-1. These are the recombinant IL-1 receptor antagonist anakinra, the neutralizing IL-1β antibody canakinumab and the soluble decoy IL-1 receptor rilonacept. These approaches have proven successful in the treatment of CAPS, and these biologic agents have been used in clinical trials for other IL-1β-associated diseases.

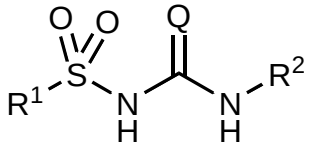
Some diarylsulfonylurea-containing compounds have been identified as cytokine release inhibitory drugs (CRIDs) (Perregaux *et al.*; J. Pharmacol. Exp. Ther. 299, 187-197, 2001). CRIDs are a class of diarylsulfonylurea-containing compounds that inhibit the post-translational processing of IL-1β. Post-translational processing of IL-1β is accompanied by activation of caspase-1 and cell death. CRIDs arrest activated monocytes so that caspase-1 remains inactive and plasma membrane latency is preserved.

Certain sulfonylurea-containing compounds are also disclosed as inhibitors of NLRP3 (see for example, Baldwin *et al.*, J. Med. Chem., 59(5), 1691-1710, 2016; and WO 2016/131098 A1, WO 2017/129897 A1, WO 2017/140778 A1, WO 2017/184604 A1, WO 2017/184623 A1, WO 2017/184624 A1 and WO 2018/015445 A1).

There is a need to provide compounds with improved pharmacological and/or physiological and/or physicochemical properties and/or those that provide a useful alternative to known compounds.

Summary

A first aspect of the disclosure provides compound of formula (I):



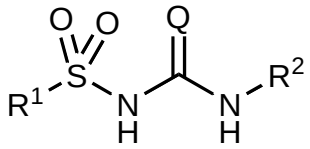
Formula (I)

wherein:

Q is selected from O or S;

R^1 is a non-aromatic heterocyclic group comprising at least one ring nitrogen atom, wherein R^1 is attached to the sulfur atom of the sulfonylurea group by a ring carbon atom, wherein R^1 may optionally be substituted, and wherein when R^1 is a partially aromatic bicyclic, tricyclic or polycyclic group, the ring of R^1 that is directly attached to the sulfur atom of the sulfonylurea group is non-aromatic; and

R^2 is a cyclic group substituted at the α-position, wherein R^2 may optionally be further substituted. An example of the disclosure provides a compound of formula (I):



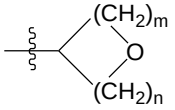
Formula (I)

wherein:

Q is selected from O or S;

R^1 is a non-aromatic heterocyclic group comprising at least one ring nitrogen atom, wherein R^1 is attached to the sulfur atom of the sulfonylurea group by a ring

In one example, R^1 is substituted on one or more (such as one, two or three) ring nitrogen atoms with a substituent independently selected from halo; C_1-C_6 alkyl; C_1-C_6 haloalkyl; C_2-C_6 alkenyl; C_2-C_6 haloalkenyl; C_2-C_6 alkynyl; C_2-C_6 haloalkynyl; -R^5-CN; -R^5-N_3; -R^5-NO_2; -R^5-$N(R^6)_2$; -R^5-OR^6; -R^5-COR^6; -R^5-$COOR^6$; -R^5-CO-R^5-OR^6; -R^5-$CON(R^6)_2$; -R^5-CO-R^5-$N(R^6)_2$; -R^5-SO_2R^6; -R^5-phenyl; -R^5-pyridinyl; -R^5-(C_3-C_6 cycloalkyl);



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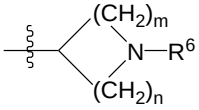


; oxo (=O); -$CH_2CH_2CH_2$-; or -$CH_2CH_2CH_2CH_2$-; wherein

R^5 is independently selected from a bond or C_1-C_5 alkylene;

R^6 is independently selected from hydrogen, C_1-C_5 alkyl, C_1-C_5 haloalkyl, C_3-C_6 cycloalkyl, -CO-(C_1-C_3 alkyl) or benzyl;

m is 1, 2 or 3; and

n is 1, 2 or 3.

In one example, R^1 is substituted on one or more (such as one, two or three) ring carbon atoms with a substituent independently selected from oxo (=O); -CH_2CH_2-; -$CH_2CH_2CH_2$-; -$CH_2CH_2CH_2CH_2$-; -CH=CH-CH=CH_2-; -OR^7 or -$CON(R^7)_2$; wherein R^7 is independently selected from hydrogen or C_1-C_3 alkyl.

In one example, R^1 is substituted on one or more (such as one, two or three) ring carbon atoms with a substituent independently selected from oxo (=O); -$CH_2CH_2CH_2$-; -$CH_2CH_2CH_2CH_2$-; or -CH=CH-CH=CH_2-.

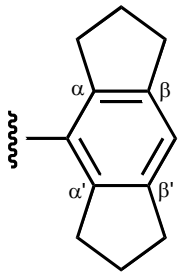
In one example of any of the above examples, R^1 contains from 4 to 25 atoms other than hydrogen. More typically, R^1 contains from 4 to 20 atoms other than hydrogen. More typically, R^1 contains from 4 to 17 atoms other than hydrogen.

R^2 is a cyclic group substituted at the α-position, wherein R^2 may optionally be further substituted. For the avoidance of doubt, it is noted that it is a ring atom of the cyclic group of R^2 that is directly attached to the nitrogen atom of the urea or thiourea group, not any substituent.

In one example of the first aspect of the disclosure, R^2 is an aryl or a heteroaryl group, wherein the aryl or the heteroaryl group is substituted at the α-position, and wherein R^2 may optionally be further substituted. Typically, R^2 is a phenyl or a 5- or 6-membered

heteroaryl group, wherein the phenyl or the heteroaryl group is substituted at the α-position, and wherein R^2 may optionally be further substituted. Typically, R^2 is an aryl or a heteroaryl group, wherein the aryl or the heteroaryl group is substituted at the α and α' positions, and wherein R^2 may optionally be further substituted. Typically, R^2 is a phenyl or a 5- or 6-membered heteroaryl group, wherein the phenyl or the heteroaryl group is substituted at the α and α' positions, and wherein R^2 may optionally be further substituted. For example, R^2 may be a phenyl group substituted at the 2- and 6-positions or a phenyl group substituted at the 2-, 4- and 6-positions.

As used herein, the nomenclature α, β, α', β' refers to the position of the atoms of a cyclic group, such as $-R^2$, relative to the point of attachment of the cyclic group to the remainder of the molecule. For example, where $-R^2$ is a 1,2,3,5,6,7-hexahydro-s-indacen-4-yl moiety, the α, β, α' and β' positions are as follows:



In another example, R^2 is a cyclic group substituted at the α and α' positions, wherein R^2 may optionally be further substituted. For example, R^2 may be a cycloalkyl, cycloalkenyl or non-aromatic heterocyclic group substituted at the α and α' positions.

In any of the above examples, typical substituents at the α and/or α' positions of the parent cyclic group of R^2 comprise a carbon atom. For example, typical substituents at the α and/or α' positions of the parent cyclic group of R^2 may be independently selected from $-R^4$, $-OR^4$ and $-COR^4$ groups, wherein each R^4 is independently selected from a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_2-C_6 cyclic group and wherein each R^4 is optionally further substituted with one or more halo groups. More typically, the substituents at the α and/or α' positions are independently selected from alkyl and cycloalkyl groups, such as C_3-C_6 branched alkyl and C_3-C_6 cycloalkyl groups, e.g. isopropyl, cyclopropyl, cyclohexyl or t-butyl groups, wherein the alkyl and cycloalkyl groups are optionally further substituted with one or more fluoro and/or chloro groups.

In one example of any of the above examples, each substituent at the α and α' positions

wherein R^4 is selected from a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_2-C_6 cyclic group and wherein R^4 is optionally substituted with one or more halo groups; and

optionally the phenyl or 5- or 6-membered heteroaryl group is further substituted (typically with one, two or three substituents independently selected from halo, $-NO_2$, -CN, $-COOR^{15}$, $-CONH_2$, $-CONHR^{15}$ or $-CON(R^{15})_2$, wherein each $-R^{15}$ is independently selected from a C_1-C_4 alkyl or C_1-C_4 haloalkyl group); or

(v) the phenyl or 5- or 6-membered heteroaryl group is substituted at the α-position with a monovalent heterocyclic group or a monovalent aromatic group selected from phenyl, pyridinyl, pyrimidinyl, pyrazolyl, imidazolyl, triazolyl or tetrahydropyranyl, wherein the monovalent heterocyclic or aromatic group may optionally be substituted with one or two substituents independently selected from halo, C_1-C_3 alkyl, C_1-C_3 haloalkyl, $-R^{12}$-OR^{13}, $-R^{12}$-$N(R^{13})_2$, $-R^{12}$-CN or $-R^{12}$-$C{\equiv}CR^{13}$, and wherein a ring atom of the monovalent heterocyclic or aromatic group is directly attached to the α-ring atom of the parent phenyl or 5- or 6-membered heteroaryl group; wherein R^{12} is independently selected from a bond or a C_1-C_3 alkylene group; and R^{13} is independently selected from hydrogen or a C_1-C_3 alkyl or C_1-C_3 haloalkyl group; and

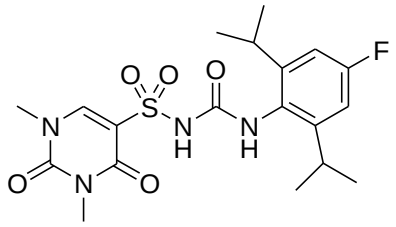
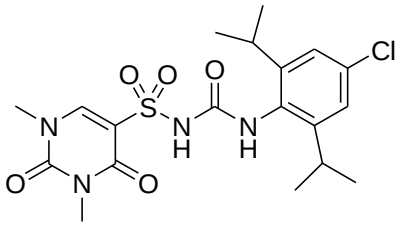
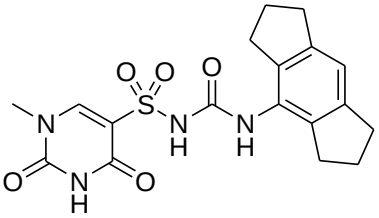
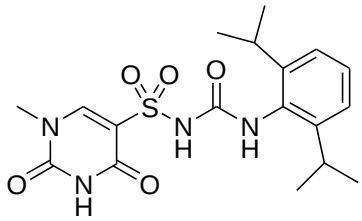
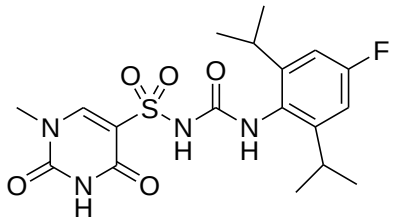
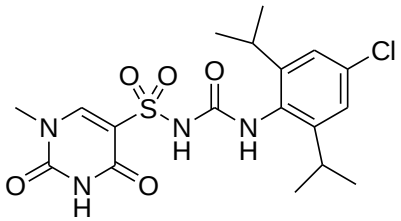
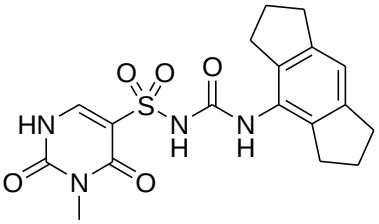
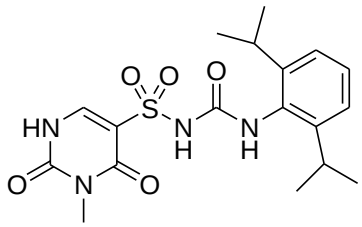
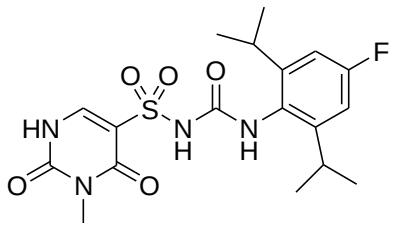
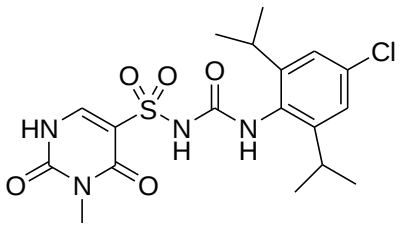
optionally the phenyl or 5- or 6-membered heteroaryl group is further substituted with a cycloalkyl, cycloalkenyl, non-aromatic heterocyclic, aryl or heteroaryl ring which is fused to the parent phenyl or 5- or 6-membered heteroaryl group across the α',β' positions and which is optionally substituted with one or more halo groups; and

optionally the phenyl or 5- or 6-membered heteroaryl group is further substituted (typically with one or two substituents independently selected from halo, $-NO_2$, -CN, $-COOR^{15}$, $-CONH_2$, $-CONHR^{15}$ or $-CON(R^{15})_2$, wherein each $-R^{15}$ is independently selected from a C_1-C_4 alkyl or C_1-C_4 haloalkyl group).

In the example directly above, where a group or moiety is optionally substituted with one or more halo groups, it may be substituted for example with one, two, three, four, five or six halo groups.

In one example of any of the above examples, R^2 contains from 15 to 50 atoms. More typically, R^2 contains from 20 to 40 atoms. Most typically, R^2 contains from 25 to 35 atoms.

In another example of any of the above examples, R^2 contains from 10 to 50 atoms other than hydrogen. More typically, R^2 contains from 10 to 40 atoms other than

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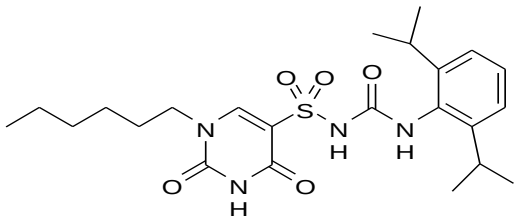
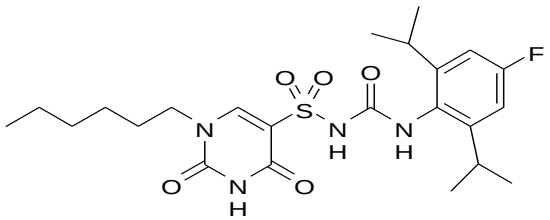
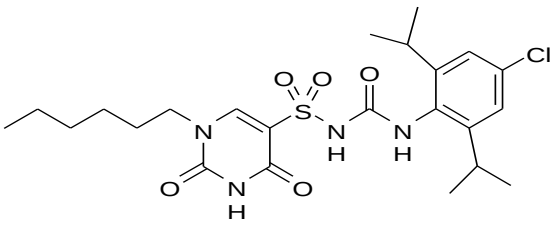
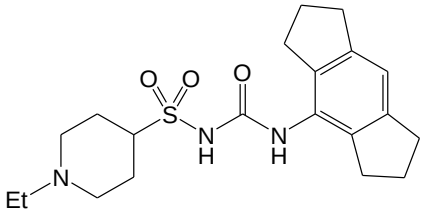




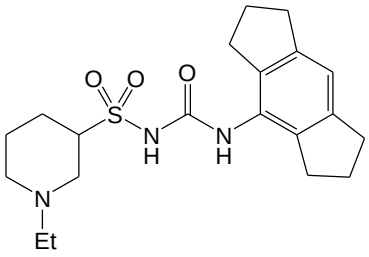
and .

The second aspect further provides a compound selected from the group consisting of:



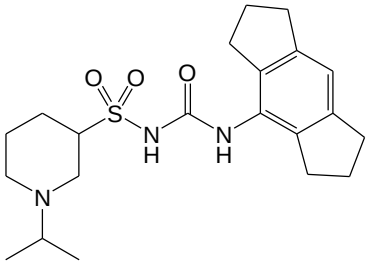
, and pharmaceutically acceptable salts and solvates thereof.

The second aspect further provides a compound selected from the group consisting of:



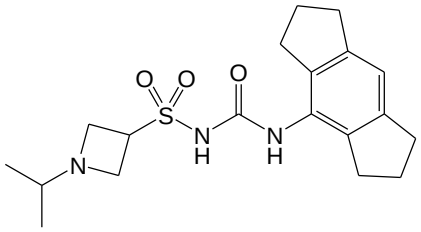
, and pharmaceutically acceptable salts and solvates thereof.

The second aspect further provides a compound selected from the group consisting of:



, and pharmaceutically acceptable salts and solvates thereof.

The second aspect further provides a compound selected from the group consisting of:



, and pharmaceutically acceptable salts and solvates thereof.

A third aspect of the disclosure provides a pharmaceutically acceptable salt, solvate or

and ^{127}I, and any radioisotope including, but not limited to ^{11}C, ^{14}C, ^{3}H (T), ^{13}N, ^{15}O, ^{18}F, ^{123}I, ^{124}I, ^{125}I and ^{131}I.

The compounds, salts, solvates and prodrugs of the present disclosure may be in any polymorphic or amorphous form.

A fourth aspect of the disclosure provides a pharmaceutical composition comprising a compound of the first or second aspect of the disclosure, or a pharmaceutically acceptable salt or solvate of the third aspect of the disclosure, and a pharmaceutically acceptable excipient. An example of the disclosure provides a pharmaceutical composition comprising a compound of the first or second aspect of the disclosure, or a pharmaceutically acceptable salt, solvate or prodrug of the third aspect of the disclosure, and a pharmaceutically acceptable excipient.

Conventional procedures for the selection and preparation of suitable pharmaceutical formulations are described in, for example, “Aulton’s Pharmaceutics - The Design and Manufacture of Medicines”, M. E. Aulton and K. M. G. Taylor, Churchill Livingstone Elsevier, 4th Ed., 2013.

Pharmaceutically acceptable excipients including adjuvants, diluents or carriers that may be used in the pharmaceutical compositions of the disclosure are those conventionally employed in the field of pharmaceutical formulation, and include, but are not limited to, sugars, sugar alcohols, starches, ion exchangers, alumina, aluminium stearate, lecithin, serum proteins such as human serum albumin, buffer substances such as phosphates, glycerine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, water, salts or electrolytes such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, zinc salts, colloidal silica, magnesium trisilicate, polyvinylpyrrolidone, cellulose-based substances, polyethylene glycol, sodium carboxymethylcellulose, polyacrylates, waxes, polyethylene-polyoxypropylene-block polymers, polyethylene glycol and wool fat.

In one example, the pharmaceutical composition of the fourth aspect of the disclosure additionally comprises one or more further active agents.

In a further example, the pharmaceutical composition of the fourth aspect of the

disclosure may be provided as a part of a kit of parts, wherein the kit of parts comprises the pharmaceutical composition of the fourth aspect of the disclosure and one or more further pharmaceutical compositions, wherein the one or more further pharmaceutical compositions each comprise a pharmaceutically acceptable excipient and one or more further active agents.

A fifth aspect of the disclosure provides a compound of the first or second aspect of the disclosure, or a pharmaceutically acceptable salt or solvate of the third aspect of the disclosure, or a pharmaceutical composition of the fourth aspect of the disclosure, for use in medicine. An example of the disclosure provides a compound of the first or second aspect of the disclosure, or a pharmaceutically acceptable salt, solvate or prodrug of the third aspect of the disclosure, or a pharmaceutical composition of the fourth aspect of the disclosure, for use in medicine, and/or for use in the treatment or prevention of a disease, disorder or condition. Typically, the use comprises the administration of the compound, salt, solvate, prodrug or pharmaceutical composition to a subject. In one example, the use comprises the co-administration of one or more further active agents.

In yet another aspect, the present disclosure provides the use of a compound as described herein, or a pharmaceutically acceptable salt or solvate as described herein, or a pharmaceutical composition as described herein, in the manufacture of a medicament for treating or preventing a disease, disorder or condition selected from:

(i) inflammation;
(ii) an auto-immune disease;
(iii) cancer;
(iv) an infection;
(v) a central nervous system disease;
(vi) a metabolic disease;
(vii) a cardiovascular disease;
(viii) a respiratory disease;
(ix) a liver disease;
(x) a renal disease;
(xi) an ocular disease;
(xii) a skin disease;
(xiii) a lymphatic condition;
(xiv) a psychological disorder;
(xv) graft versus host disease; and
(xvi) allodynia.

In yet another aspect, the present disclosure provides the use of a compound as described herein, or a pharmaceutically acceptable salt or solvate as described herein, or a pharmaceutical composition as described herein, in the manufacture of a medicament for treating or preventing a disease, disorder or condition selected from:

(i) cryopyrin-associated periodic syndromes (CAPS);
(ii) Muckle-Wells syndrome (MWS);
(iii) familial cold autoinflammatory syndrome (FCAS);
(iv) neonatal onset multisystem inflammatory disease (NOMID);
(v) familial Mediterranean fever (FMF);
(vi) pyogenic arthritis, pyoderma gangrenosum and acne syndrome (PAPA);
(vii) hyperimmunoglobulinemia D and periodic fever syndrome (HIDS);
(viii) Tumour Necrosis Factor (TNF) Receptor-Associated Periodic Syndrome (TRAPS);
(ix) systemic juvenile idiopathic arthritis;
(x) adult-onset Still's disease (AOSD);
(xi) relapsing polychondritis;
(xii) Schnitzler's syndrome;
(xiii) Sweet's syndrome;
(xiv) Behcet's disease;
(xv) anti-synthetase syndrome;
(xvi) deficiency of interleukin 1 receptor antagonist (DIRA); and
(xvii) haploinsufficiency of A20 (HA20).

The term "treatment" as used herein refers equally to curative therapy, and ameliorating or palliative therapy. The term includes obtaining beneficial or desired physiological results, which may or may not be established clinically. Beneficial or desired clinical results include, but are not limited to, the alleviation of symptoms, the prevention of symptoms, the diminishment of extent of disease, the stabilisation (i.e., not worsening) of a condition, the delay or slowing of progression/worsening of a condition/symptoms, the amelioration or palliation of the condition/symptoms, and remission (whether partial or total), whether detectable or undetectable. The term "palliation", and variations thereof, as used herein, means that the extent and/or undesirable manifestations of a physiological condition or symptom are lessened and/or time course of the progression is slowed or lengthened, as compared to not administering a compound, salt, solvate, prodrug or pharmaceutical composition of the present disclosure. The term "prevention" as used herein in relation to a disease, disorder or condition, relates to prophylactic or preventative therapy, as well as therapy to reduce the risk of developing the disease, disorder or condition. The term "prevention" includes both the avoidance of occurrence of the disease, disorder or condition, and the delay in onset of the disease, disorder or condition. Any statistically

significant ($p \leq 0.05$) avoidance of occurrence, delay in onset or reduction in risk as measured by a controlled clinical trial may be deemed a prevention of the disease, disorder or condition. Subjects amenable to prevention include those at heightened risk of a disease, disorder or condition as identified by genetic or biochemical markers. Typically, the genetic or biochemical markers are appropriate to the disease, disorder or condition under consideration and may include for example, inflammatory biomarkers such as C-reactive protein (CRP) and monocyte chemoattractant protein 1 (MCP-1) in the case of inflammation; total cholesterol, triglycerides, insulin resistance and C-peptide in the case of NAFLD and NASH; and more generally IL1β and IL18 in the case of a disease, disorder or condition responsive to NLRP3 inhibition.

A further example of the disclosure provides the use of a compound of the first or second aspect, or a pharmaceutically effective salt, solvate or prodrug of the third aspect, in the manufacture of a medicament for the treatment or prevention of a disease, disorder or condition. Typically, the treatment or prevention comprises the administration of the compound, salt, solvate, prodrug or medicament to a subject. In one example, the treatment or prevention comprises the co-administration of one or more further active agents.

A further example of the disclosure provides a method of treatment or prevention of a disease, disorder or condition, the method comprising the step of administering an effective amount of a compound of the first or second aspect, or a pharmaceutically acceptable salt, solvate or prodrug of the third aspect, or a pharmaceutical composition of the fourth aspect, to thereby treat or prevent the disease, disorder or condition. In one example, the method further comprises the step of co-administering an effective amount of one or more further active agents. Typically, the administration is to a subject in need thereof.

A further aspect provides a compound of the first or second aspect, or a pharmaceutically acceptable salt or solvate of the third aspect, or a pharmaceutical composition of the fourth aspect, for use in inhibiting NLRP3. A further example of the disclosure provides a compound of the first or second aspect of the disclosure, or a pharmaceutically acceptable salt, solvate or prodrug of the third aspect of the disclosure, or a pharmaceutical composition of the fourth aspect of the disclosure, for use in the treatment or prevention of a disease, disorder or condition in an individual, wherein the individual has a germline or somatic non-silent mutation in NLRP3. The

mutation may be, for example, a gain-of-function or other mutation resulting in increased NLRP3 activity. Typically, the use comprises the administration of the compound, salt, solvate, prodrug or pharmaceutical composition to the individual. In one example, the use comprises the co-administration of one or more further active agents. The use may also comprise the diagnosis of an individual having a germline or somatic non-silent mutation in NLRP3, wherein the compound, salt, solvate, prodrug or pharmaceutical composition is administered to an individual on the basis of a positive diagnosis for the mutation. Typically, identification of the mutation in NLRP3 in the individual may be by any suitable genetic or biochemical means.

A further example of the disclosure provides the use of a compound of the first or second aspect, or a pharmaceutically effective salt, solvate or prodrug of the third aspect, in the manufacture of a medicament for the treatment or prevention of a disease, disorder or condition in an individual, wherein the individual has a germline or somatic non-silent mutation in NLRP3. The mutation may be, for example, a gain-of-function or other mutation resulting in increased NLRP3 activity. Typically, the treatment or prevention comprises the administration of the compound, salt, solvate, prodrug or medicament to the individual. In one example, the treatment or prevention comprises the co-administration of one or more further active agents. The treatment or prevention may also comprise the diagnosis of an individual having a germline or somatic non-silent mutation in NLRP3, wherein the compound, salt, solvate, prodrug or medicament is administered to an individual on the basis of a positive diagnosis for the mutation. Typically, identification of the mutation in NLRP3 in the individual may be by any suitable genetic or biochemical means.

A further example of the disclosure provides a method of treatment or prevention of a disease, disorder or condition, the method comprising the steps of diagnosing of an individual having a germline or somatic non-silent mutation in NLRP3, and administering an effective amount of a compound of the first or second aspect, or a pharmaceutically acceptable salt, solvate or prodrug of the third aspect, or a pharmaceutical composition of the fourth aspect, to the positively diagnosed individual, to thereby treat or prevent the disease, disorder or condition. In one example, the method further comprises the step of co-administering an effective amount of one or more further active agents. Typically, the administration is to a subject in need thereof.

In general examples, the disease, disorder or condition may be a disease, disorder or condition of the immune system, the cardiovascular system, the endocrine system, the gastrointestinal tract, the renal system, the hepatic system, the metabolic system, the

hypersensitivity pneumonitis, or idiopathic interstitial pneumonia;

(vi) a vascular condition such as atherosclerosis, Behcet's disease, vasculitides, or wegener's granulomatosis;

(vii) an autoimmune condition such as systemic lupus erythematosus, Sjogren's syndrome, systemic sclerosis, Hashimoto's thyroiditis, type I diabetes, idiopathic thrombocytopenia purpura, or Graves disease;

(viii) an ocular condition such as uveitis, allergic conjunctivitis, or vernal conjunctivitis;

(ix) a nervous condition such as multiple sclerosis or encephalomyelitis;

(x) an infection or infection-related condition, such as Acquired Immunodeficiency Syndrome (AIDS), acute or chronic bacterial infection, acute or chronic parasitic infection, acute or chronic viral infection, acute or chronic fungal infection, meningitis, hepatitis (A, B or C, or other viral hepatitis), peritonitis, pneumonia, epiglottitis, malaria, dengue hemorrhagic fever, leishmaniasis, streptococcal myositis, mycobacterium tuberculosis, mycobacterium avium intracellulare, pneumocystis carinii pneumonia, orchitis/epidydimitis, legionella, Lyme disease, influenza A, epstein-barr virus, viral encephalitis/aseptic meningitis, or pelvic inflammatory disease;

(xi) a renal condition such as mesangial proliferative glomerulonephritis, nephrotic syndrome, nephritis, glomerular nephritis, acute renal failure, uremia, or nephritic syndrome;

(xii) a lymphatic condition such as Castleman's disease;

(xiii) a condition of, or involving, the immune system, such as hyper IgE syndrome, lepromatous leprosy, familial hemophagocytic lymphohistiocytosis, or graft versus host disease;

(xiv) a hepatic condition such as chronic active hepatitis, non-alcoholic steatohepatitis (NASH), alcohol-induced hepatitis, non-alcoholic fatty liver disease (NAFLD), alcoholic fatty liver disease (AFLD), alcoholic steatohepatitis (ASH) or primary biliary cirrhosis;

(xv) a cancer, including those cancers listed above;

(xvi) a burn, wound, trauma, haemorrhage or stroke;

(xvii) radiation exposure; and/or

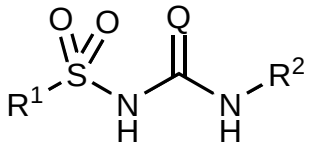
(xviii) obesity; and/or

(xix) pain such as inflammatory hyperalgesia.

In one example of the present disclosure, the disease, disorder or condition is an

Claims

1. A compound of formula (I):



Formula (I)

wherein:

Q is selected from O or S;

R^1 is a non-aromatic heterocyclic group comprising at least one ring nitrogen atom, wherein R^1 is attached to the sulfur atom of the sulfonylurea group by a ring carbon atom, wherein R^1 may optionally be substituted, and wherein when R^1 is a partially aromatic bicyclic, tricyclic or polycyclic group, the ring of R^1 that is directly attached to the sulfur atom of the sulfonylurea group is non-aromatic; and

R^2 is a cyclic group substituted at the α-position, wherein R^2 may optionally be further substituted.

2. A compound as claimed in claim 1, wherein R^1 is a monocyclic or bicyclic non-aromatic heterocyclic group, wherein R^1 may optionally be substituted.

3. A compound as claimed in claim 2, wherein R^1 is a 4-, 5-, 6- or 7-membered monocyclic non-aromatic heterocyclic group or a 7-, 8-, 9- or 10-membered bicyclic non-aromatic heterocyclic group, wherein R^1 may optionally be substituted.

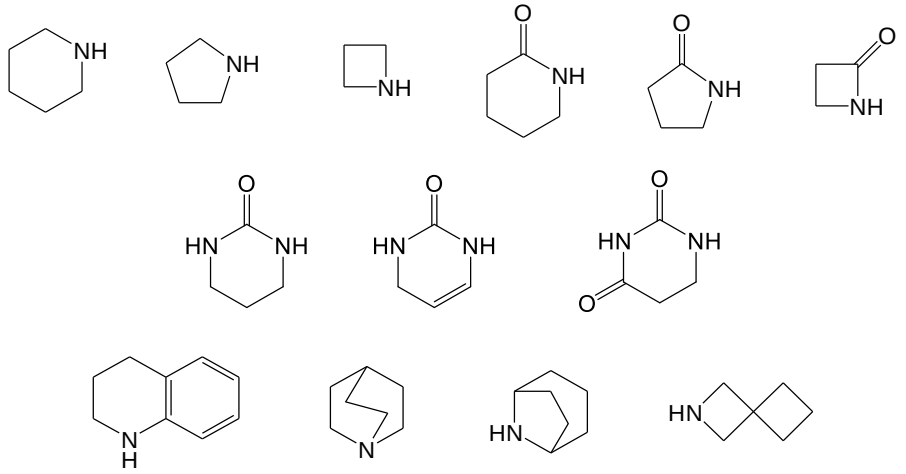
4. A compound as claimed in any one of claims 1 to 3, wherein the non-aromatic heterocyclic group of R^1 is fully saturated.

5. A compound as claimed in any one of claims 1 to 4, wherein R^1 comprises one, two or three ring nitrogen, oxygen or sulfur atoms.

6. A compound as claimed in claim 5, wherein R^1 comprises one or two ring nitrogen or oxygen atoms.

7. A compound as claimed in claim 6, wherein R^1 comprises one or two ring nitrogen atoms.

8. A compound as claimed in any one of claims 1 to 7, wherein R^1 is selected from:



wherein R^1 is attached to the sulfur atom of the sulfonylurea group by a non-aromatic ring carbon atom, and wherein R^1 may optionally be substituted or further substituted.

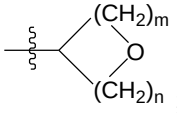
9. A compound as claimed in any one of claims 1 to 8, wherein R^1 is substituted with one or more substituents independently selected from halo; -CN; $-NO_2$; $-N_3$; $-R^\beta$; -OH; $-OR^\beta$; -SH; $-SR^\beta$; $-SOR^\beta$; $-SO_2H$; $-SO_2R^\beta$; $-SO_2NH_2$; $-SO_2NHR^\beta$; $-SO_2N(R^\beta)_2$; $-R^\alpha$-SH; $-R^\alpha$-SR^β; $-R^\alpha$-SOR^β; $-R^\alpha$-SO_2H; $-R^\alpha$-SO_2R^β; $-R^\alpha$-SO_2NH_2; $-R^\alpha$-SO_2NHR^β; $-R^\alpha$-$SO_2N(R^\beta)_2$; $-NH_2$; $-NHR^\beta$; $-N(R^\beta)_2$; $-R^\alpha$-NH_2; $-R^\alpha$-NHR^β; $-R^\alpha$-$N(R^\beta)_2$; -CHO; $-COR^\beta$; -COOH; $-COOR^\beta$; $-OCOR^\beta$; $-R^\alpha$-CHO; $-R^\alpha$-COR^β; $-R^\alpha$-COOH; $-R^\alpha$-$COOR^\beta$; $-R^\alpha$-$OCOR^\beta$; -NH-CHO; $-NR^\beta$-CHO; -NH-COR^β; $-NR^\beta$-COR^β; $-CONH_2$; $-CONHR^\beta$; $-CON(R^\beta)_2$; $-R^\alpha$-NH-CHO; $-R^\alpha$-NR^β-CHO; $-R^\alpha$-NH-COR^β; $-R^\alpha$-NR^β-COR^β; $-R^\alpha$-$CONH_2$; $-R^\alpha$-$CONHR^\beta$; $-R^\alpha$-$CON(R^\beta)_2$; -O-R^α-OH; -O-R^α-OR^β; -O-R^α-NH_2; -O-R^α-NHR^β; -O-R^α-$N(R^\beta)_2$; -NH-R^α-OH; -NH-R^α-OR^β; -NH-R^α-NH_2; -NH-R^α-NHR^β; -NH-R^α-$N(R^\beta)_2$; $-NR^\beta$-R^α-OH; $-NR^\beta$-R^α-OR^β; $-NR^\beta$-R^α-NH_2; $-NR^\beta$-R^α-NHR^β; $-NR^\beta$-R^α-$N(R^\beta)_2$; a C_3-C_7 cycloalkyl group optionally substituted with one or more C_1-C_3 alkyl or C_1-C_3 haloalkyl groups; a C_3-C_7 cycloalkenyl group optionally substituted with one or more C_1-C_3 alkyl or C_1-C_3 haloalkyl groups; a 3- to 7-membered non-aromatic heterocyclic group optionally substituted with one or more C_1-C_6 alkyl or C_1-C_3 haloalkyl groups; oxo (=O); or a C_1-C_4 alkylene bridge;

wherein each $-R^\alpha-$ is independently selected from an alkylene, alkenylene or alkynylene group, wherein the alkylene, alkenylene or alkynylene group contains from 1 to 6 atoms in its backbone, wherein one or more carbon atoms in the backbone of the alkylene, alkenylene or alkynylene group may optionally be replaced by one or more

heteroatoms N, O or S, and wherein the alkylene, alkenylene or alkynylene group may optionally be substituted with one or more halo and/or -R^{β} groups; and

wherein each -R^{β} is independently selected from a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_2-C_6 cyclic group, and wherein any -R^{β} may optionally be substituted with one or more C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_3-C_7 cycloalkyl, -O(C_1-C_3 alkyl), halo, -CN, -C≡CH or oxo (=O) groups.

10. A compound as claimed in claim 9, wherein R^1 is substituted on one or more ring nitrogen atoms with a substituent independently selected from halo; -CN; -NO_2; -N_3; -R^{β}; -OH; -OR^{β}; -SH; -SR^{β}; -SOR^{β}; -SO_2H; -SO_2R^{β}; -SO_2NH_2; -SO_2NHR^{β}; -$SO_2N(R^{\beta})_2$; -R^{α}-SH; -R^{α}-SR^{β}; -R^{α}-SOR^{β}; -R^{α}-SO_2H; -R^{α}-SO_2R^{β}; -R^{α}-SO_2NH_2; -R^{α}-SO_2NHR^{β}; -R^{α}-$SO_2N(R^{\beta})_2$; -NH_2; -NHR^{β}; -$N(R^{\beta})_2$; -R^{α}-NH_2; -R^{α}-NHR^{β}; -R^{α}-$N(R^{\beta})_2$; -CHO; -COR^{β}; -COOH; -$COOR^{\beta}$; -$OCOR^{\beta}$; -R^{α}-CHO; -R^{α}-COR^{β}; -R^{α}-COOH; -R^{α}-$COOR^{\beta}$; -R^{α}-$OCOR^{\beta}$; -NH-CHO; -NR^{β}-CHO; -NH-COR^{β}; -NR^{β}-COR^{β}; -$CONH_2$; -$CONHR^{\beta}$; -$CON(R^{\beta})_2$; -R^{α}-NH-CHO; -R^{α}-NR^{β}-CHO; -R^{α}-NH-COR^{β}; -R^{α}-NR^{β}-COR^{β}; -R^{α}-$CONH_2$; -R^{α}-$CONHR^{\beta}$; -R^{α}-$CON(R^{\beta})_2$; a C_3-C_7 cycloalkyl group optionally substituted with one or more C_1-C_3 alkyl or C_1-C_3 haloalkyl groups; a C_3-C_7 cycloalkenyl group optionally substituted with one or more C_1-C_3 alkyl or C_1-C_3 haloalkyl groups;



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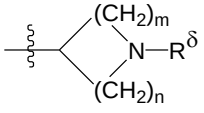


; oxo (=O); or a C_1-C_4 alkylene bridge;

wherein each -R^{α}- is independently selected from an alkylene, alkenylene or alkynylene group, wherein the alkylene, alkenylene or alkynylene group contains from 1 to 6 carbon atoms in its backbone, and wherein the alkylene, alkenylene or alkynylene group may optionally be substituted with one or more halo and/or -R^{β} groups;

wherein each -R^{β} is independently selected from a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_2-C_6 cyclic group, and wherein any -R^{β} may optionally be substituted with one or more C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_3-C_7 cycloalkyl, -O(C_1-C_3 alkyl), halo, -CN, -C≡CH or oxo (=O) groups;

wherein each -R^{δ} is independently selected from a C_1-C_6 alkyl or C_1-C_3 haloalkyl group;

wherein each m is independently selected from 1, 2 or 3; and

wherein each n is independently selected from 1, 2 or 3.

11. A compound as claimed in any one of claims 1 to 10, wherein R^2 is an aryl or a heteroaryl group, wherein the aryl or the heteroaryl group is substituted at the α-

position, and wherein R^2 may optionally be further substituted.

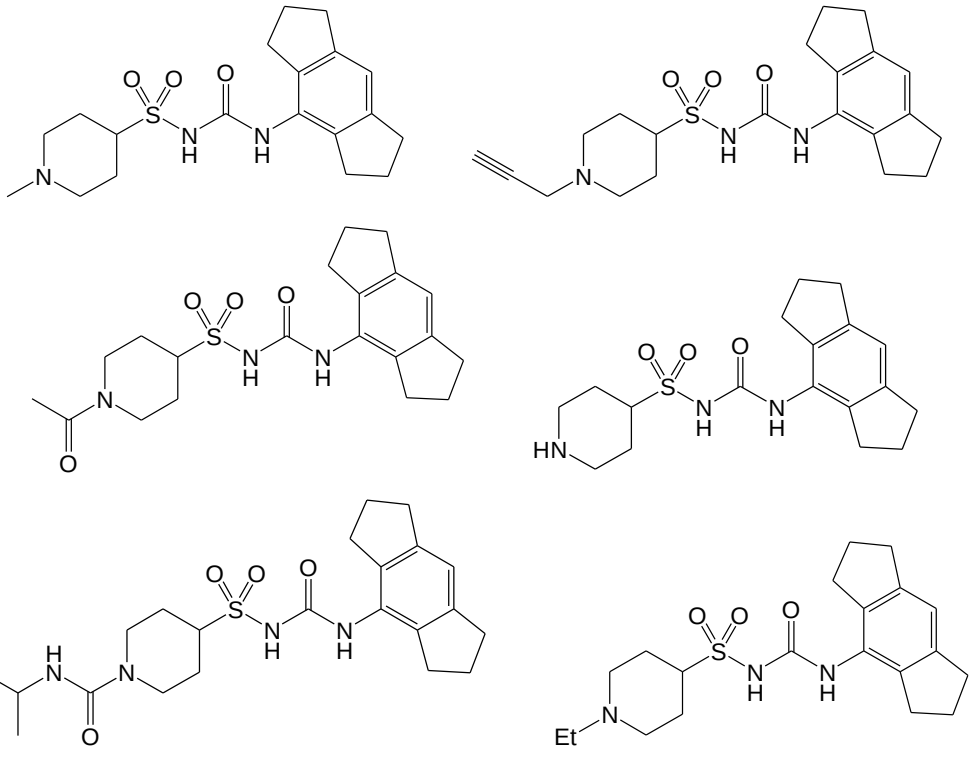
12. A compound as claimed in claim 11, wherein R^2 is an aryl or a heteroaryl group, wherein the aryl or the heteroaryl group is substituted at the α and α' positions, and wherein R^2 may optionally be further substituted.

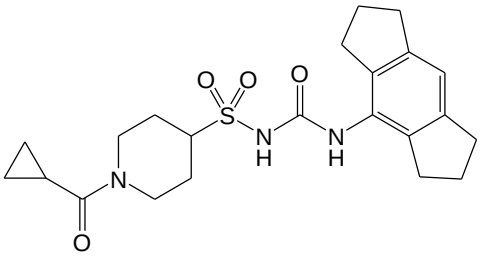
13. A compound as claimed in claim 12, wherein R^2 is a fused aryl or a fused heteroaryl group, wherein a first cycloalkyl, cycloalkenyl, non-aromatic heterocyclic, aryl or heteroaryl ring is fused to the aryl or heteroaryl group across the α,β positions and a second cycloalkyl, cycloalkenyl, non-aromatic heterocyclic, aryl or heteroaryl ring is fused to the aryl or heteroaryl group across the α',β' positions, and wherein R^2 may optionally be further substituted.

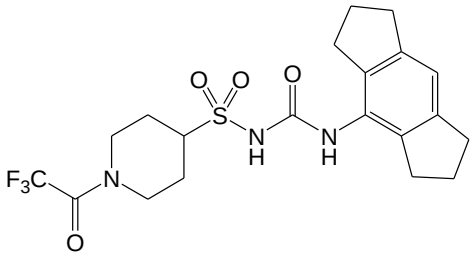
14. A compound as claimed in any one of claims 1 to 10, wherein R^2 is a cyclic group substituted at the α and α' positions, wherein R^2 may optionally be further substituted.

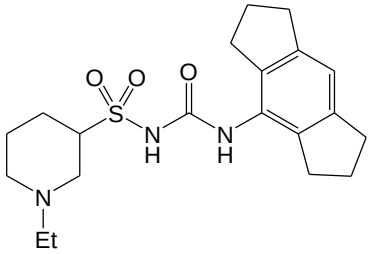
15. A compound as claimed in any one of claims 1 to 14, wherein Q is O.

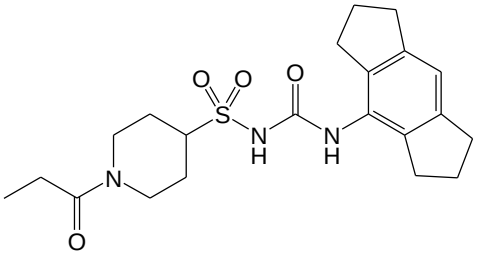
16. A compound selected from the group consisting of:

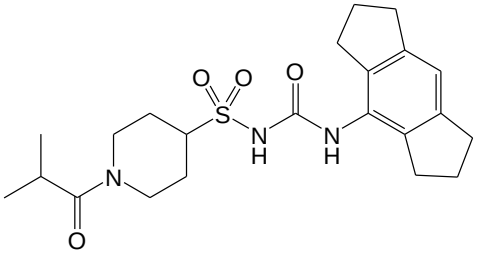


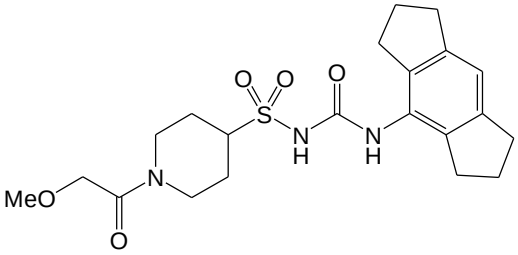


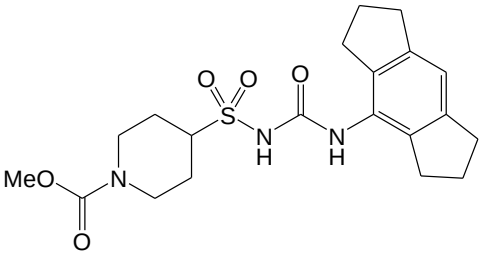


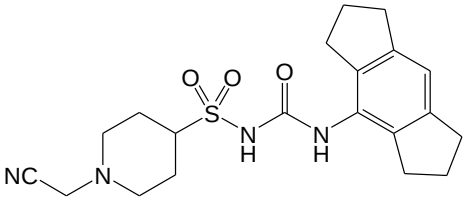


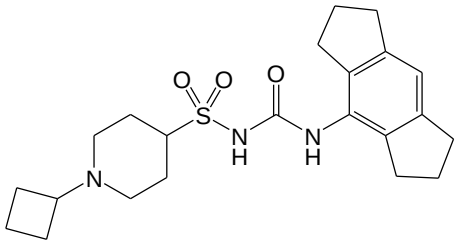


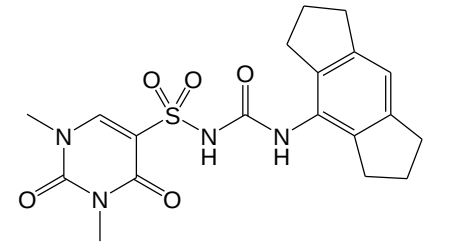


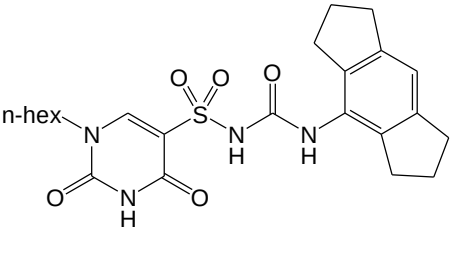












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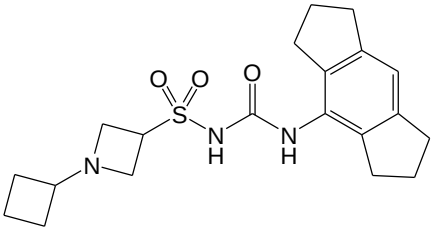

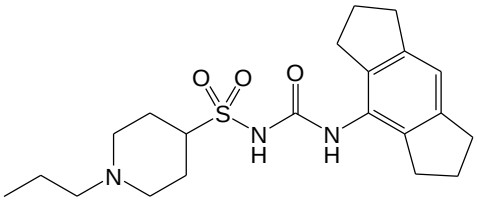

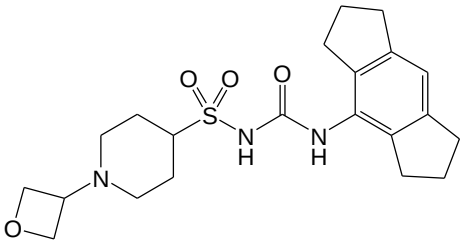

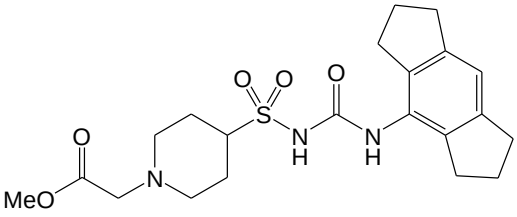

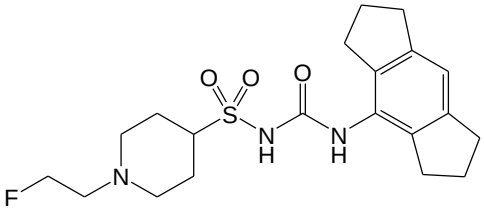

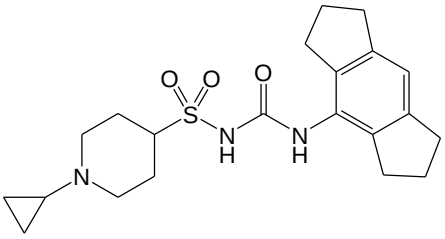

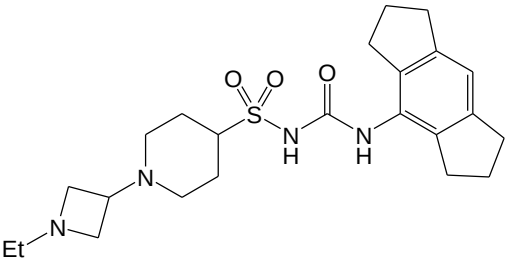

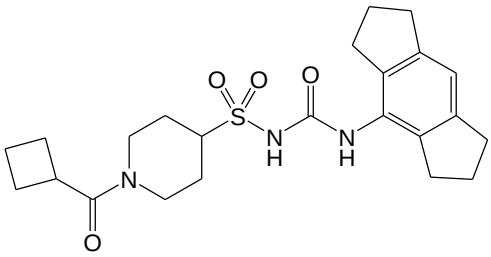

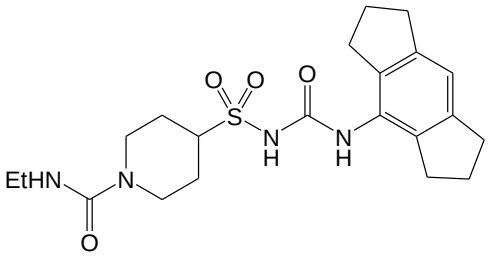

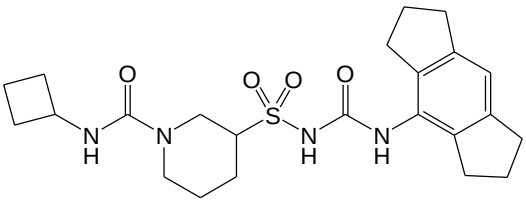

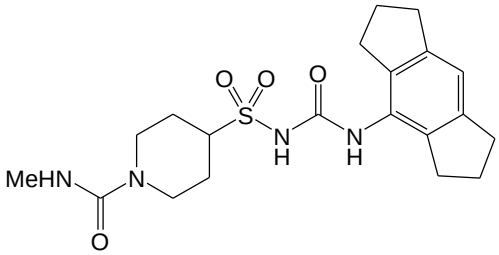

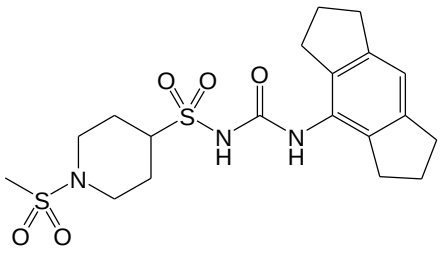

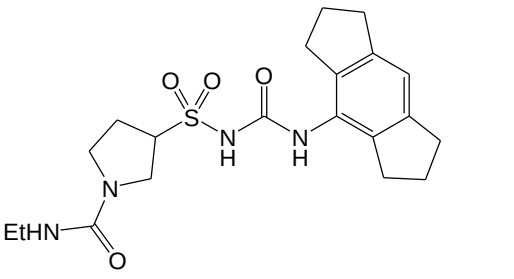

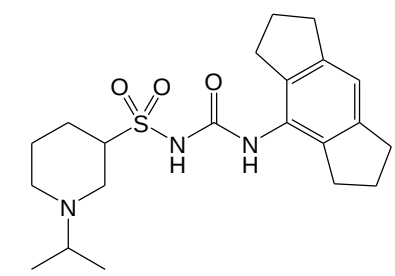

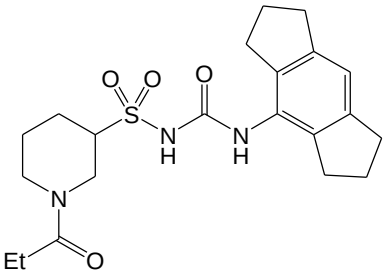

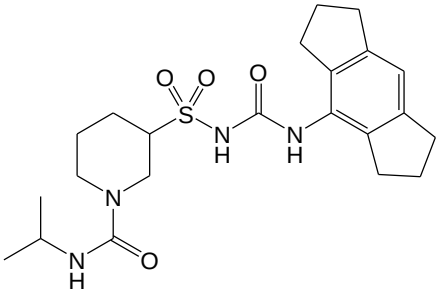

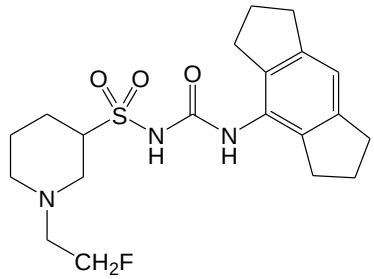

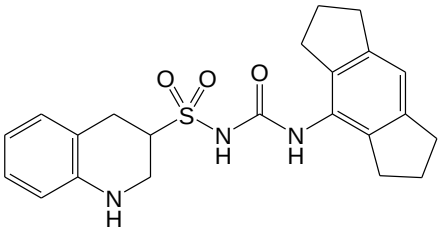

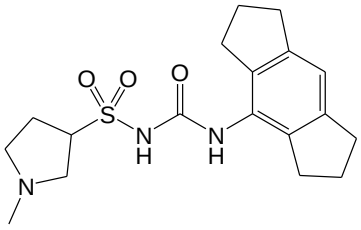

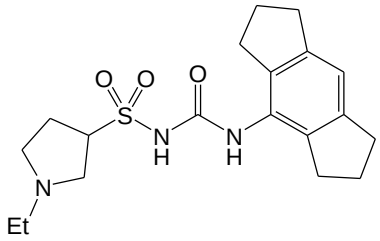

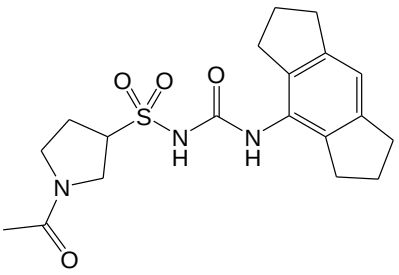

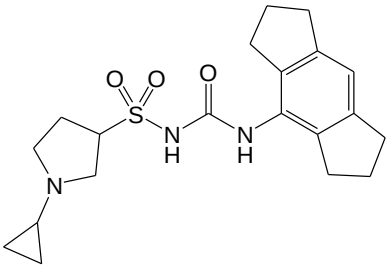

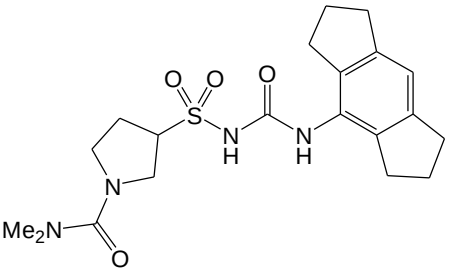

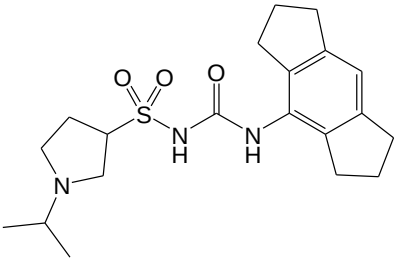

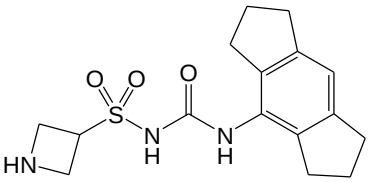

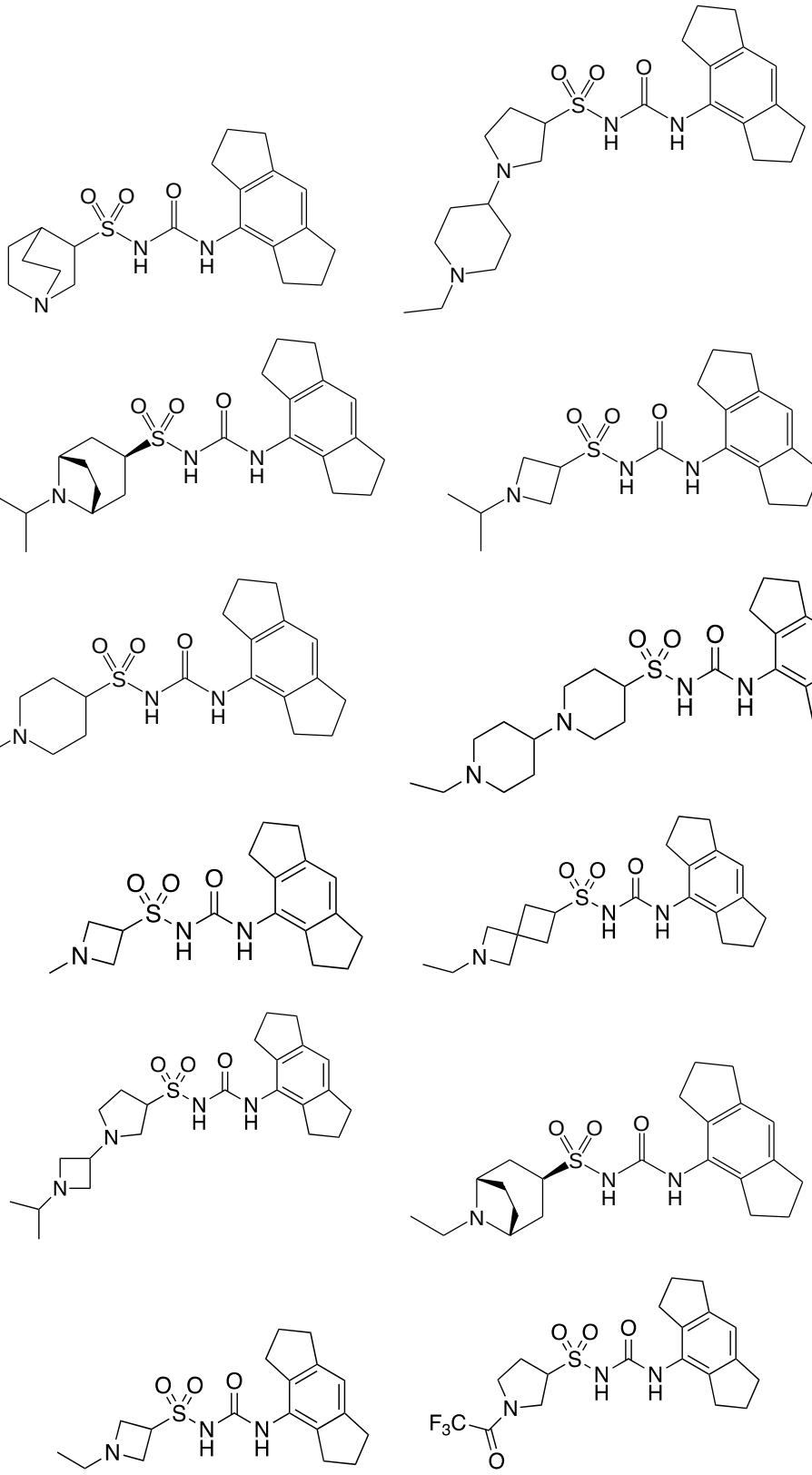

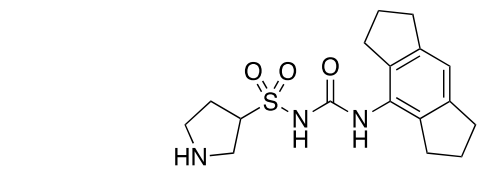

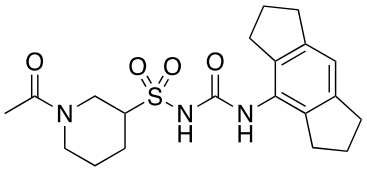

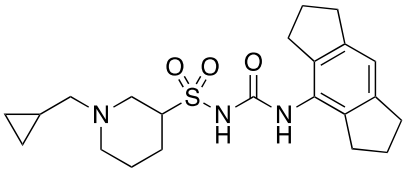

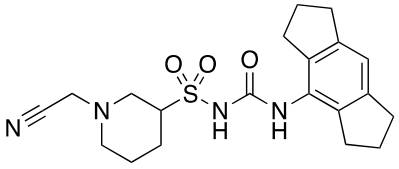

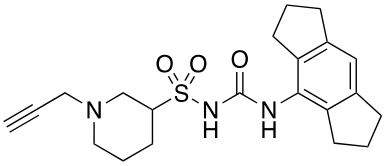

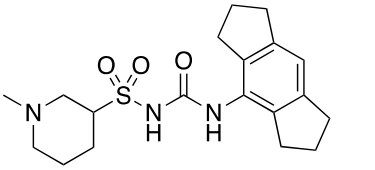

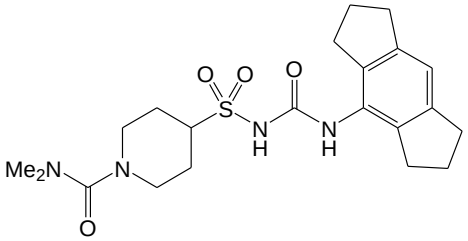

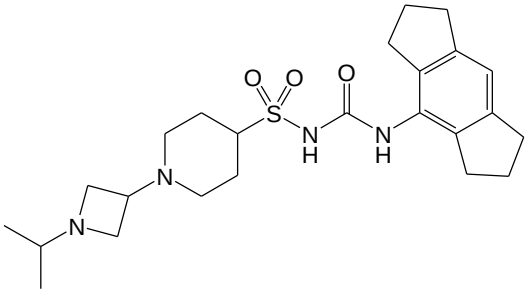

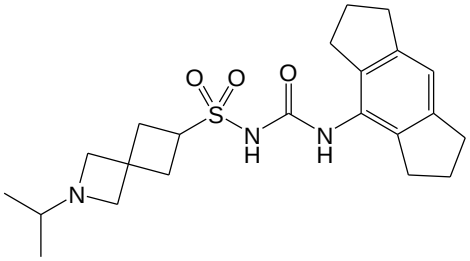

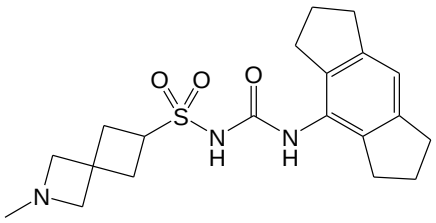

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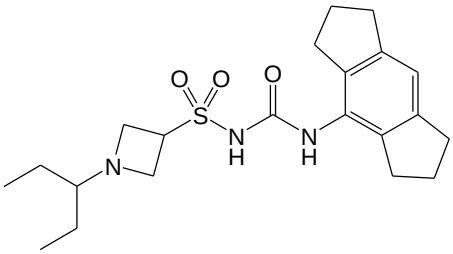

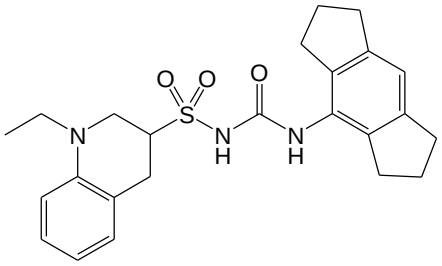

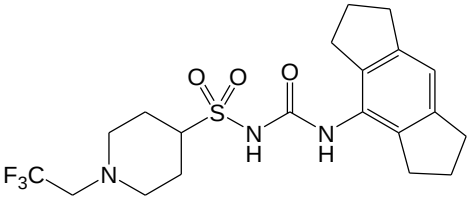

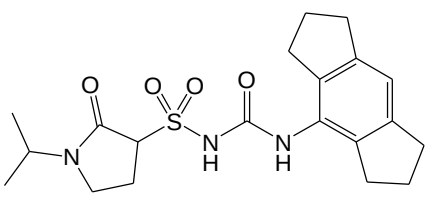

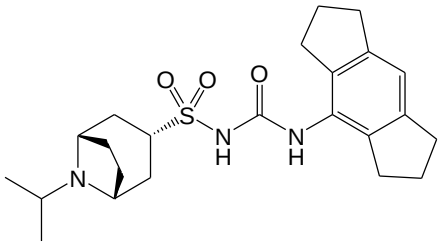

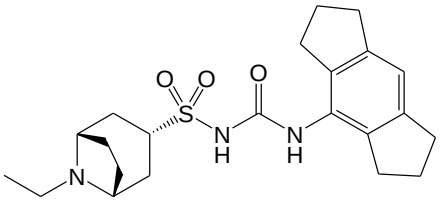

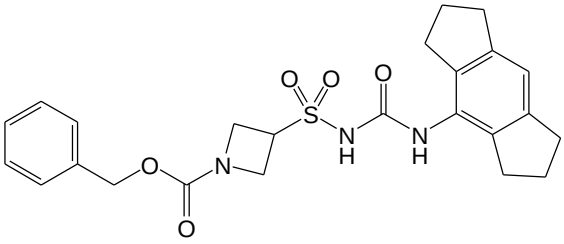

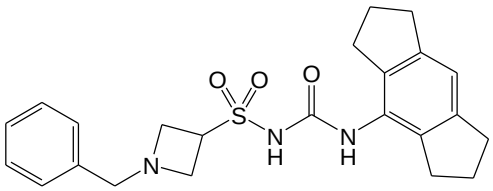

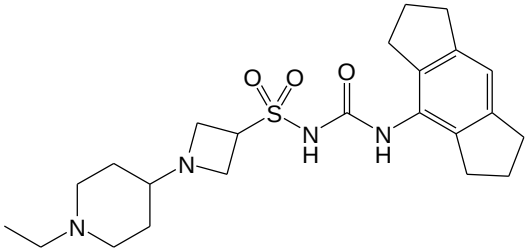

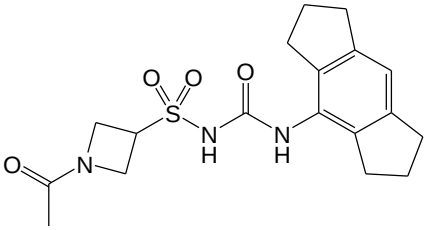

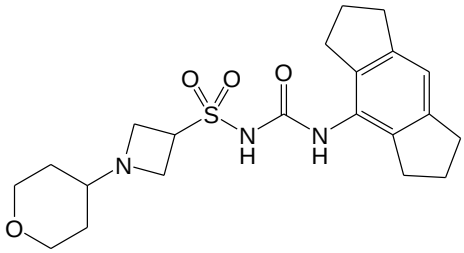

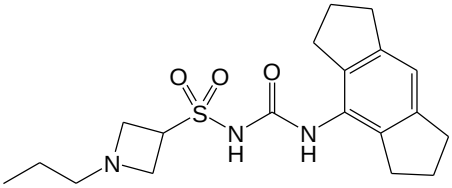

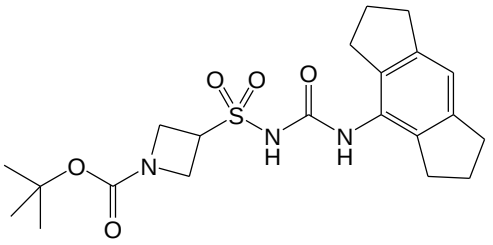

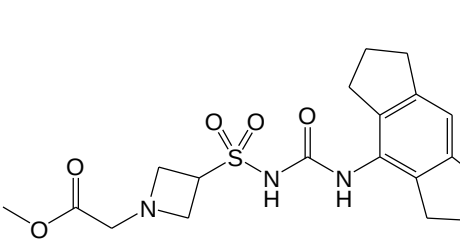

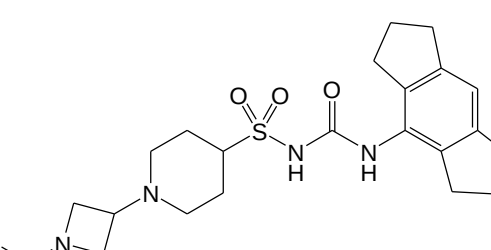

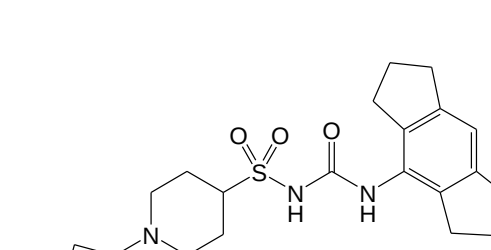

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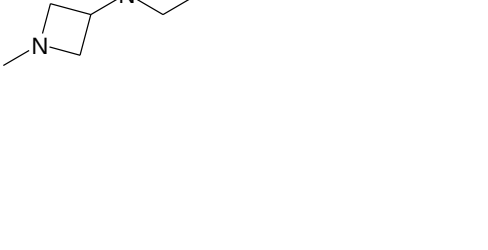

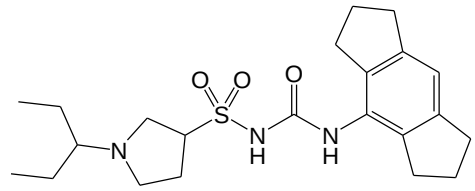

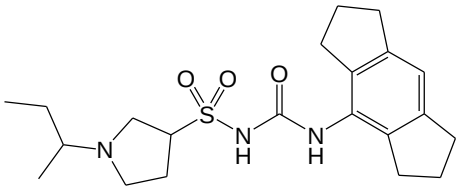

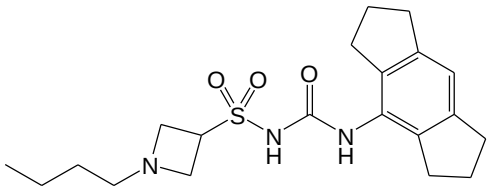

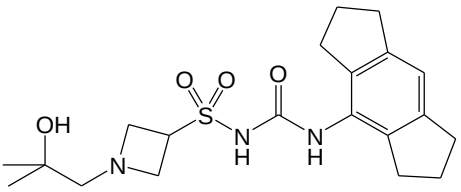

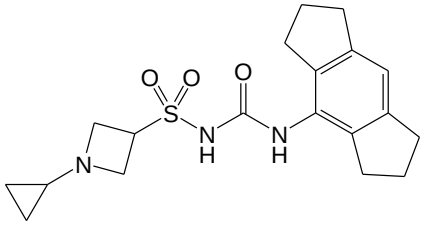

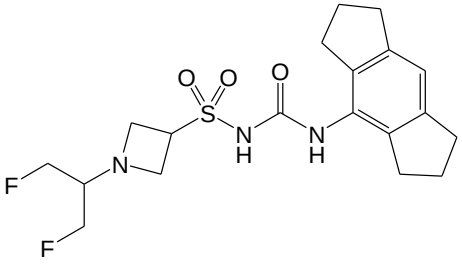

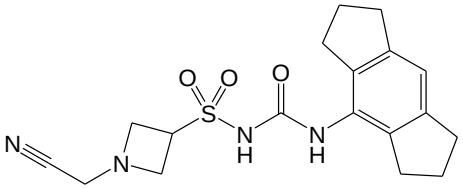

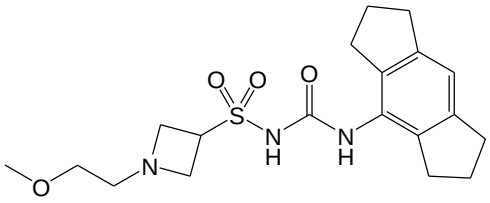

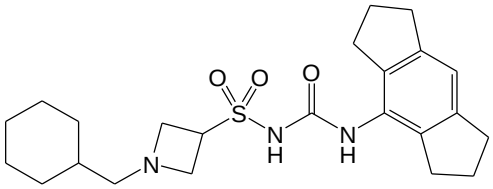

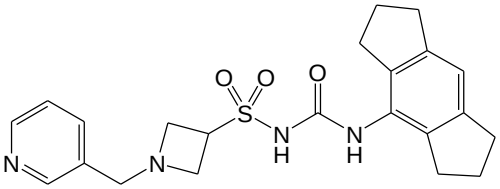

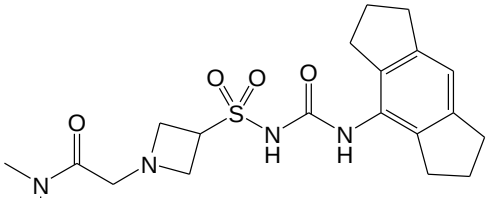

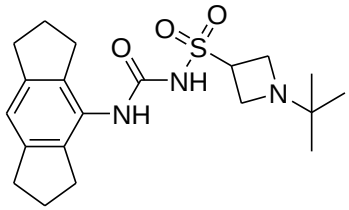

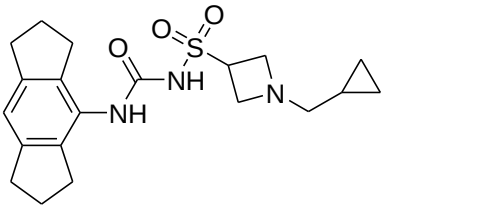

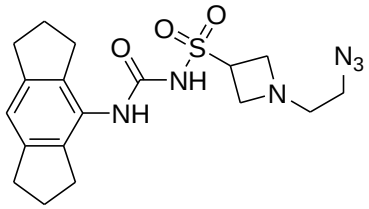

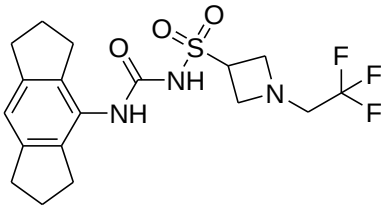

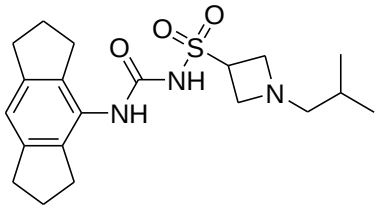

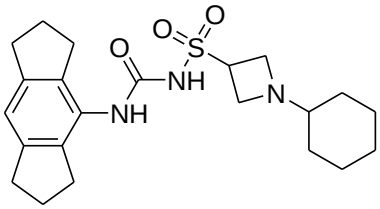

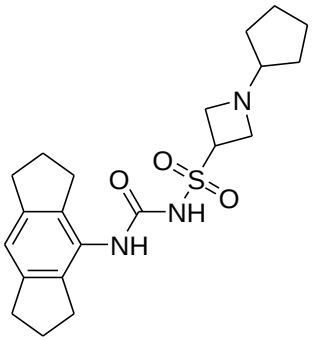

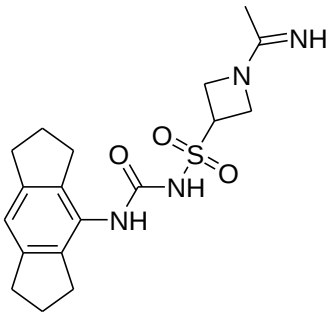

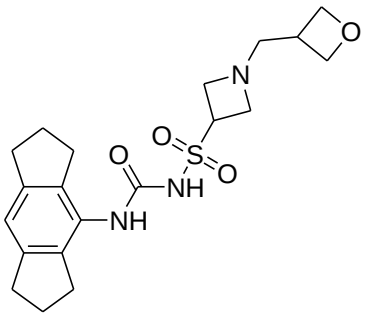

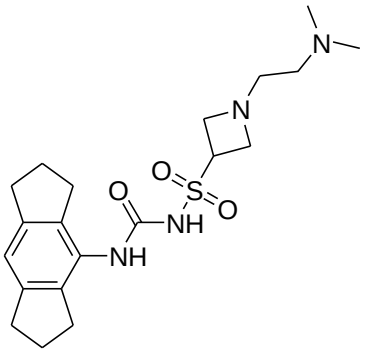

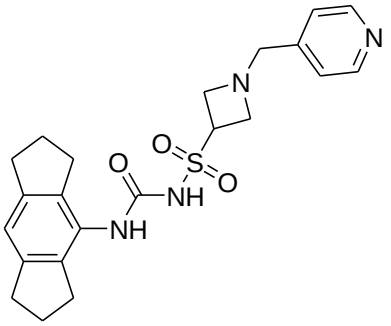

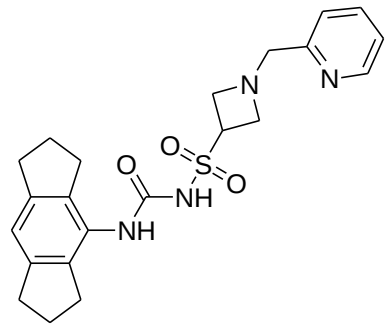

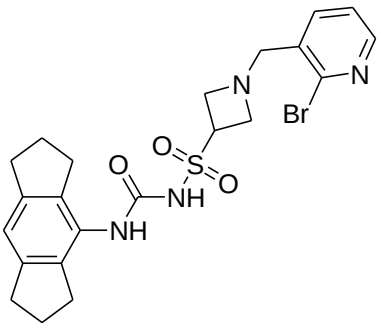

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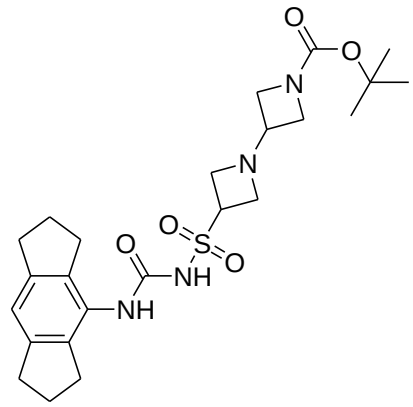

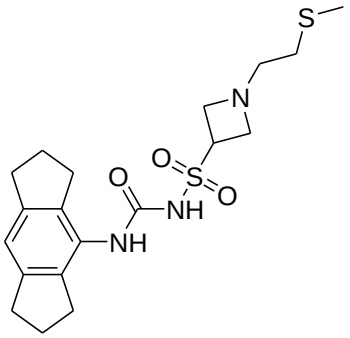

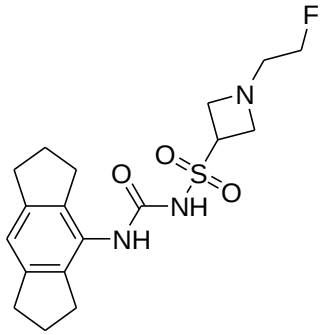

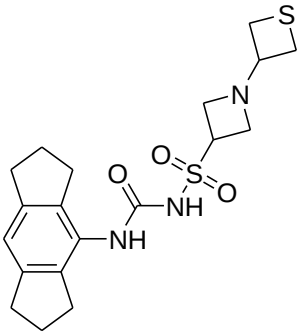

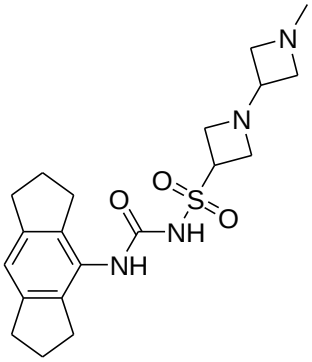

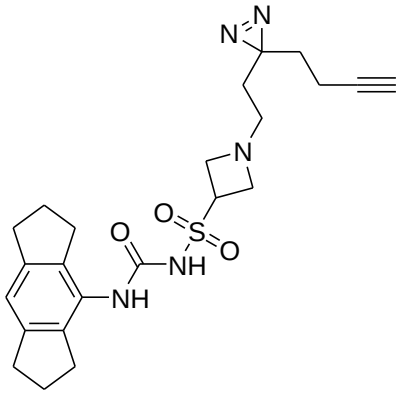

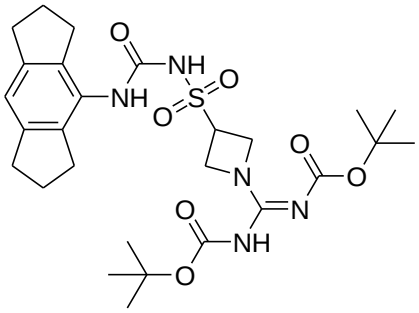

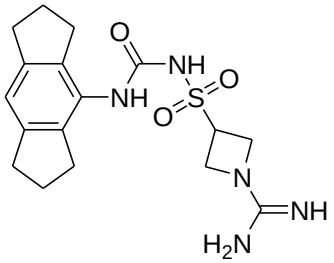

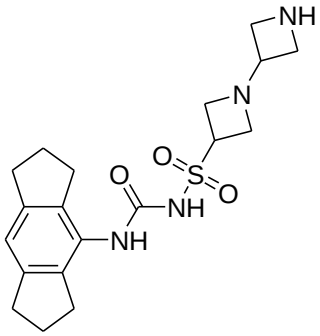

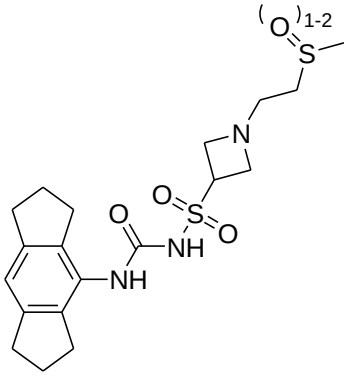

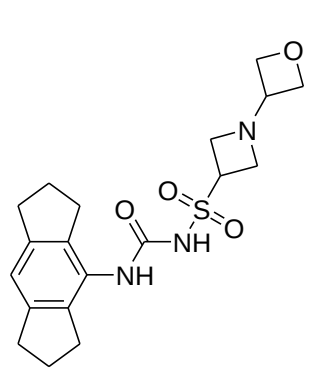
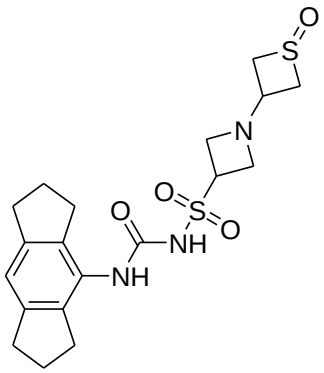
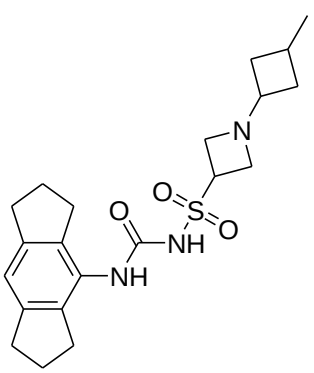
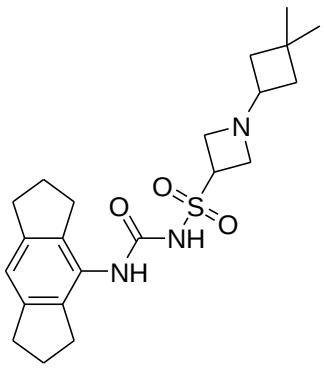
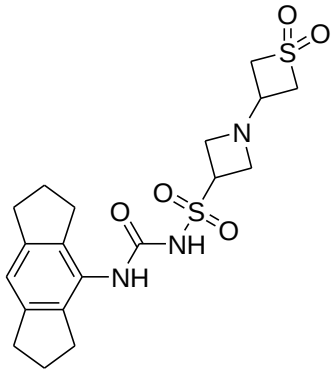
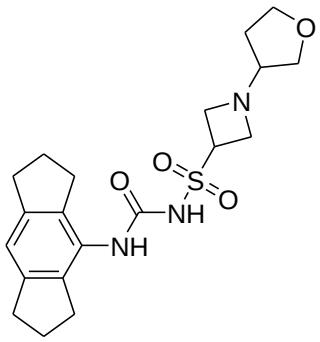
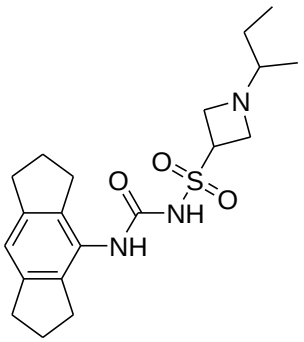
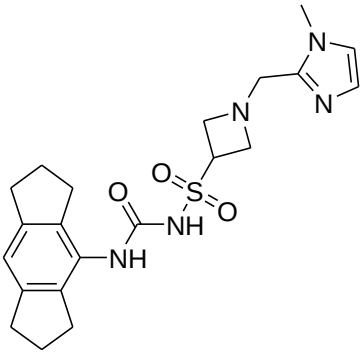
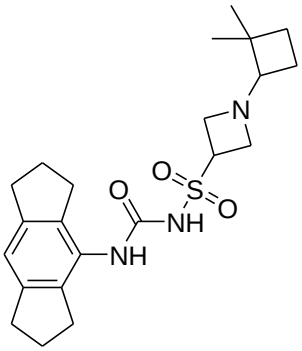
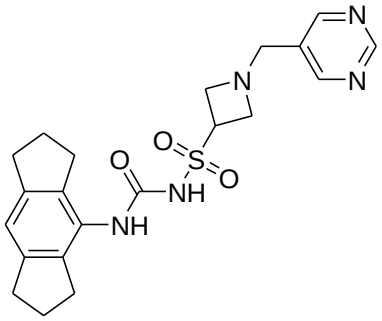
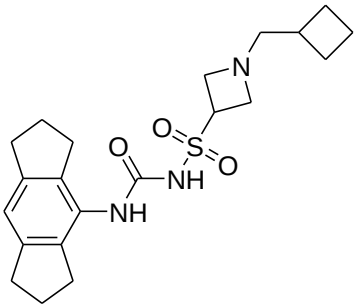

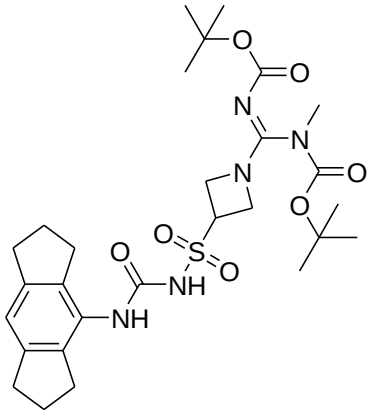

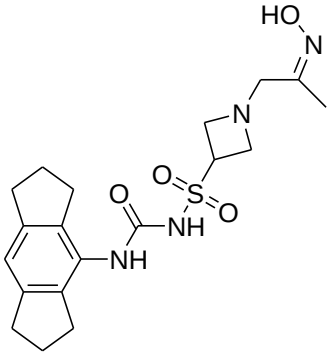

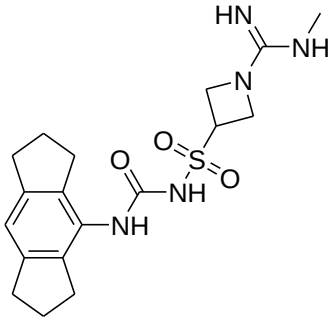

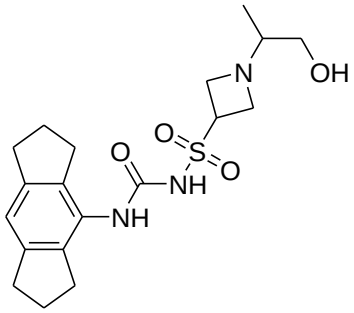

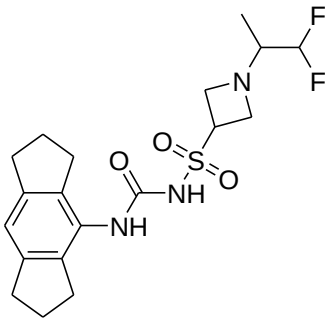

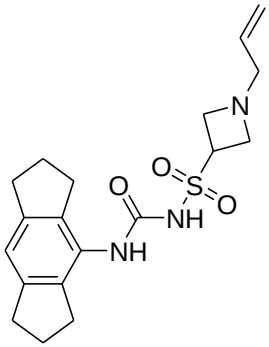

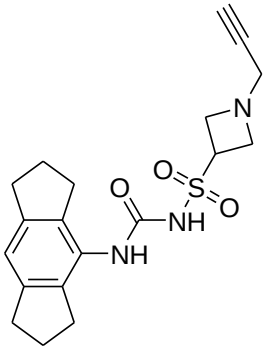

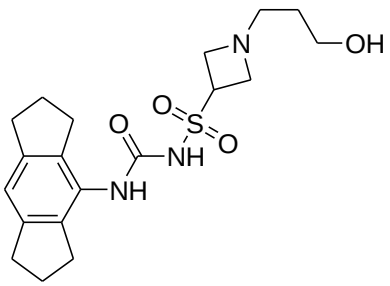

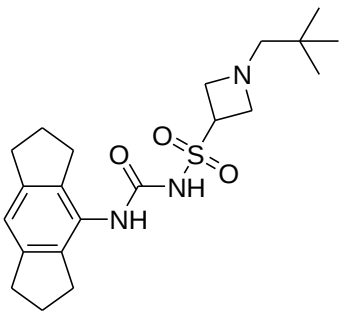

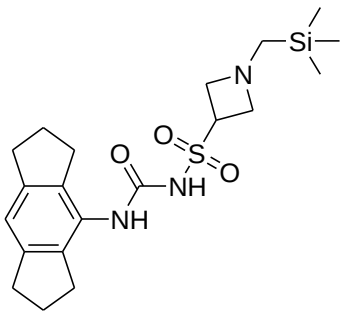

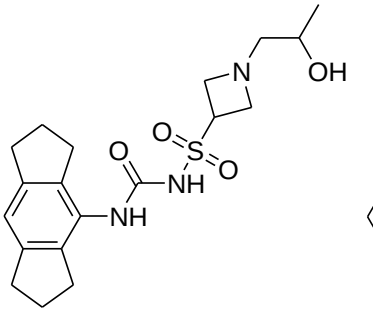

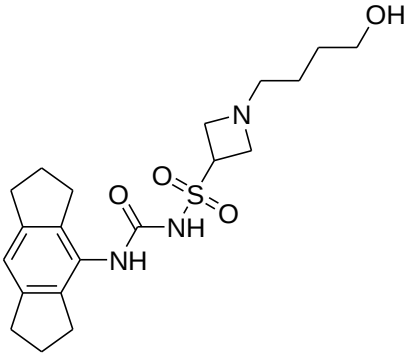

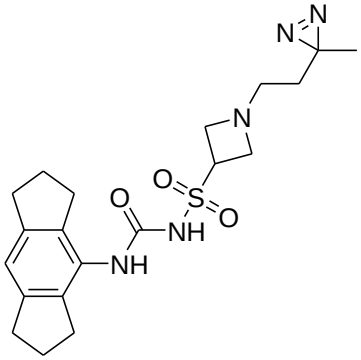

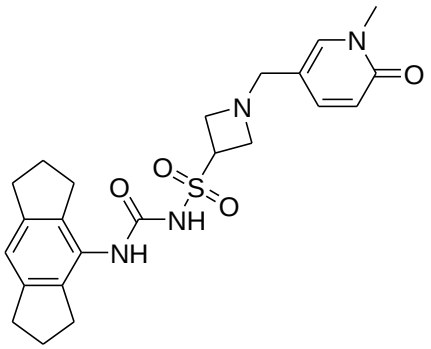

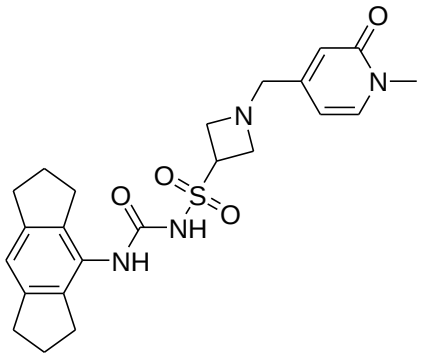

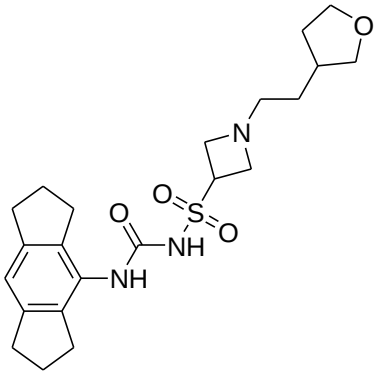

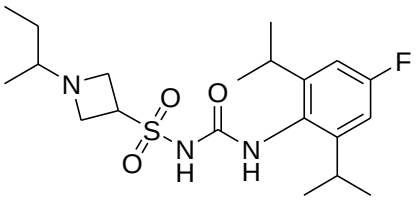

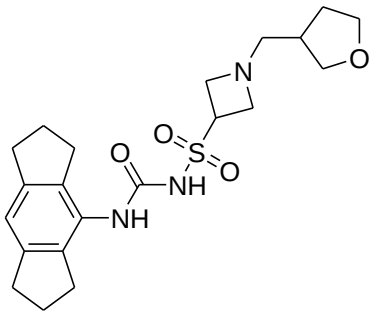

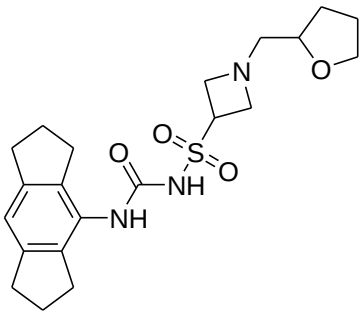

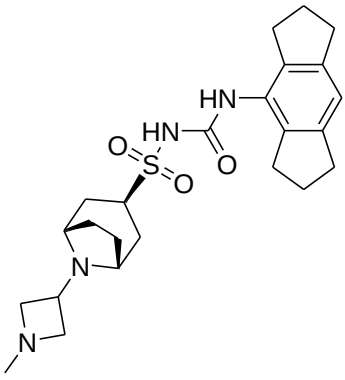

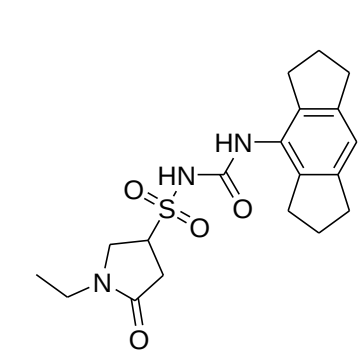

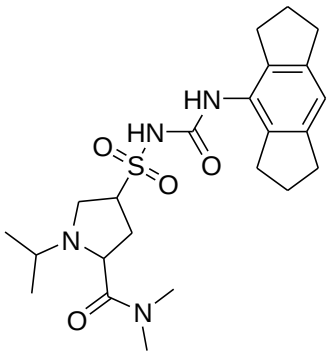

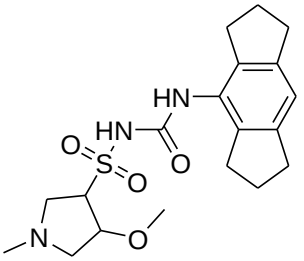

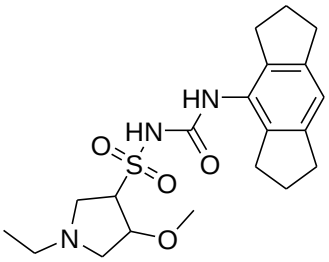

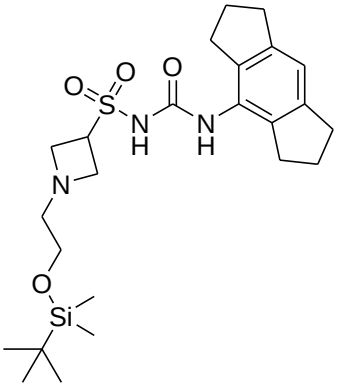

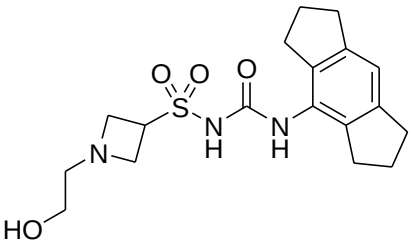

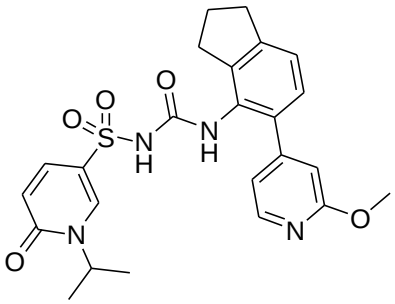

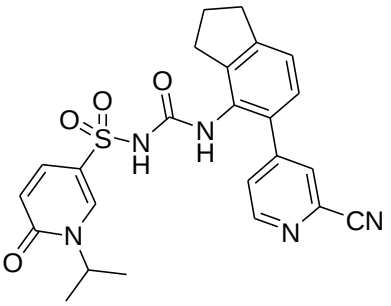

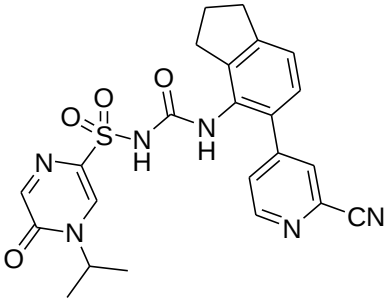

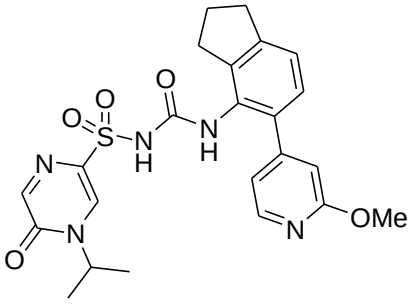

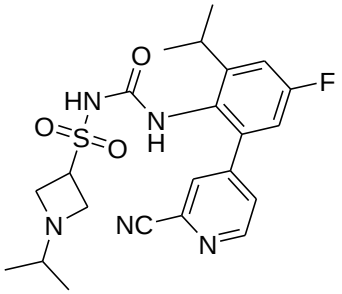

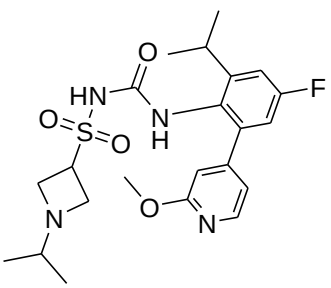

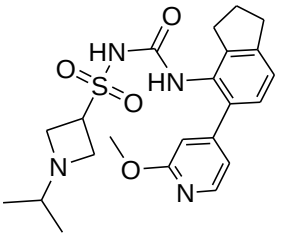

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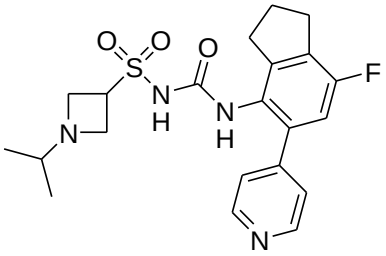

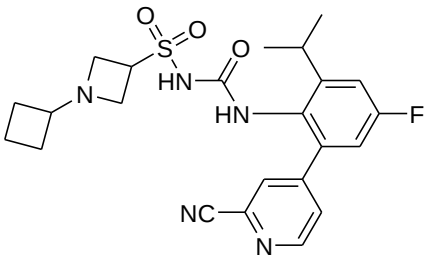

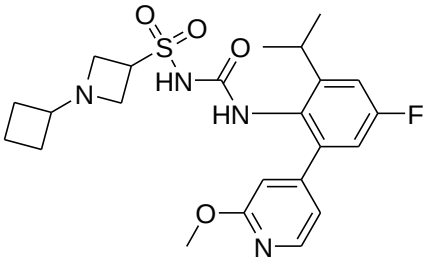

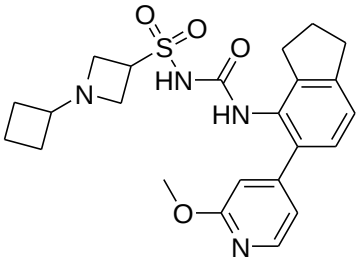

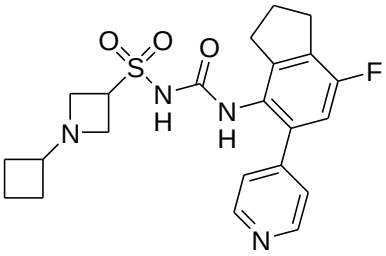

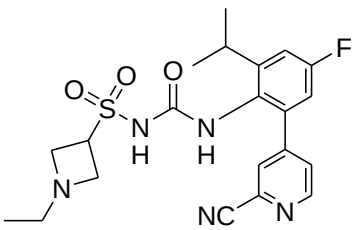

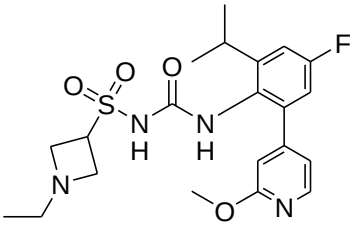

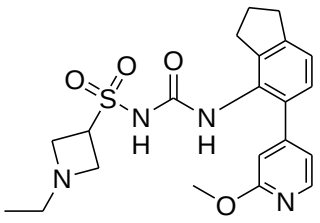

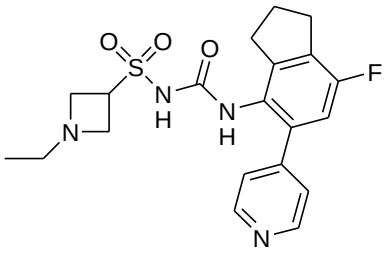

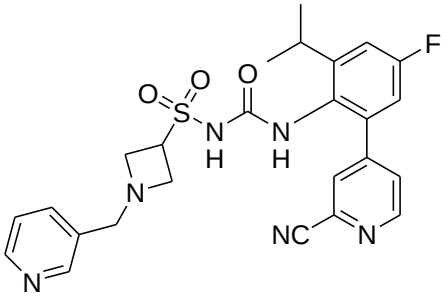

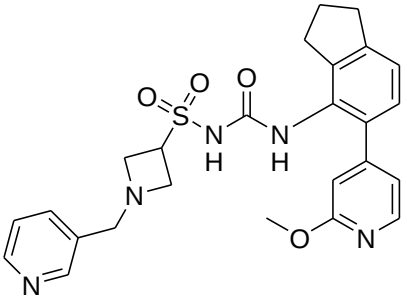

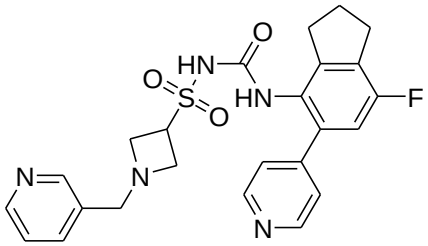

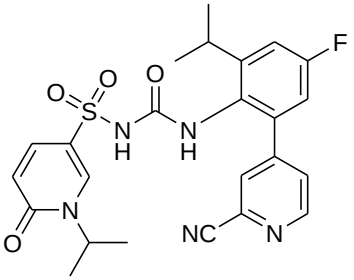

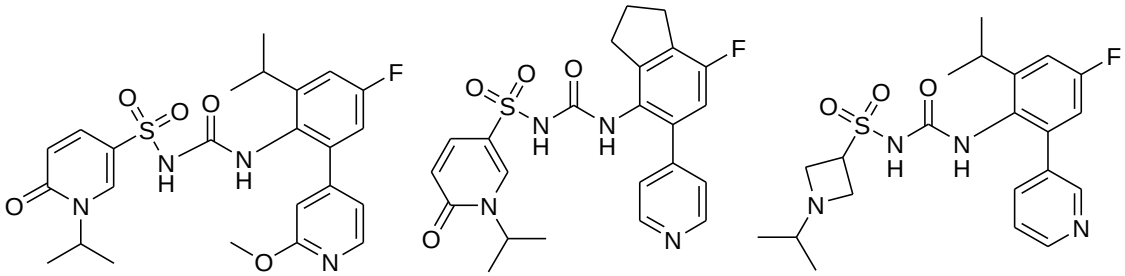

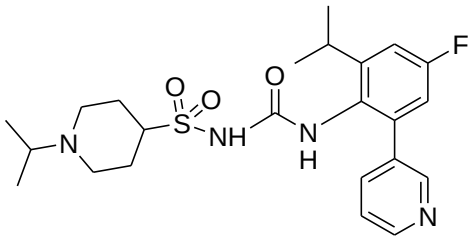

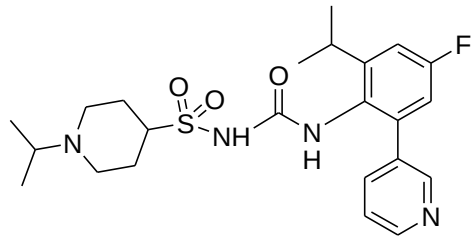

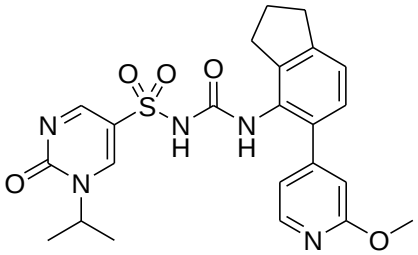

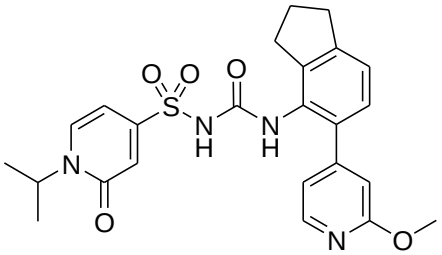

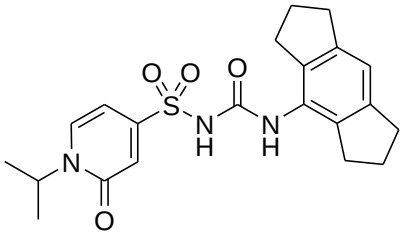

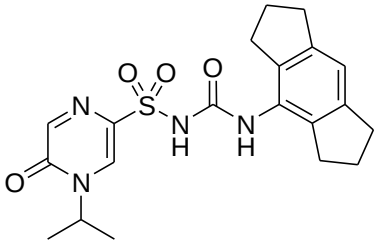

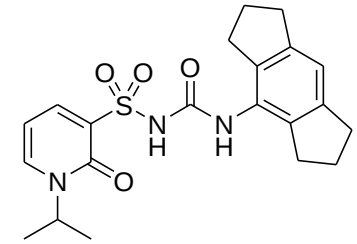

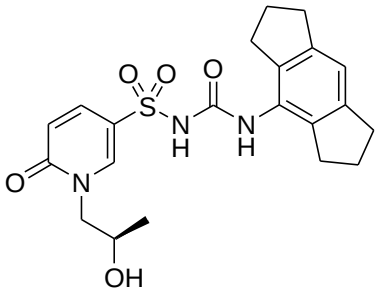

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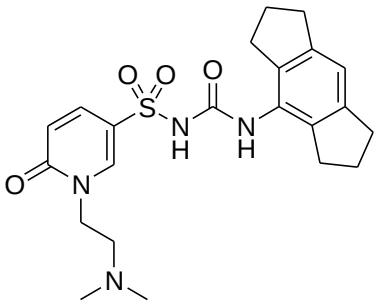

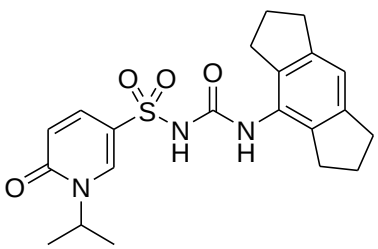

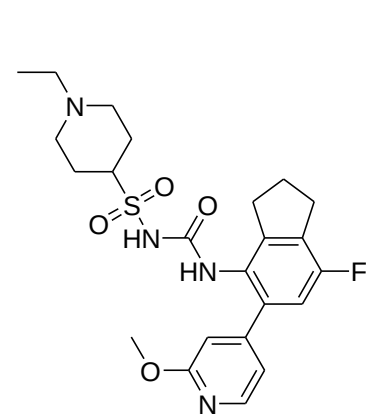
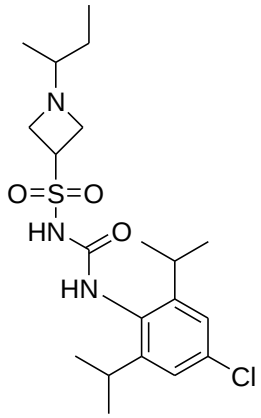
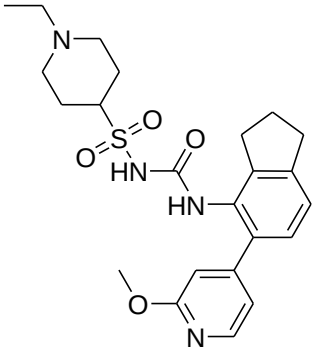
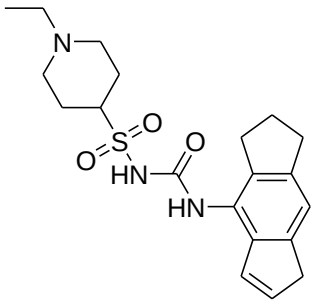
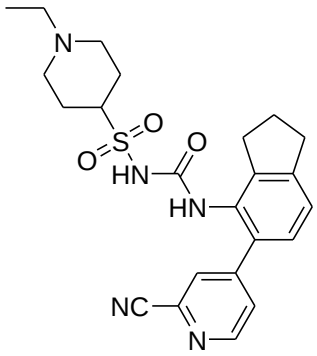
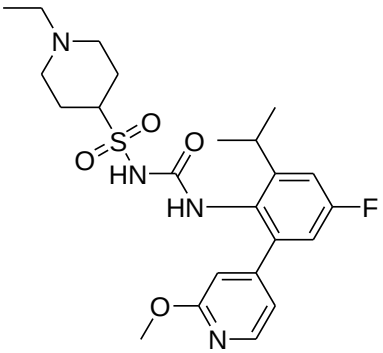
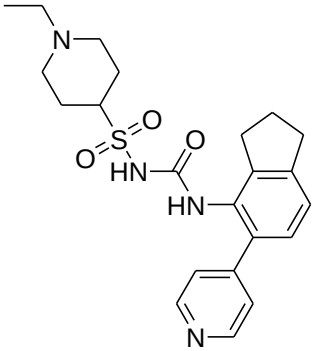
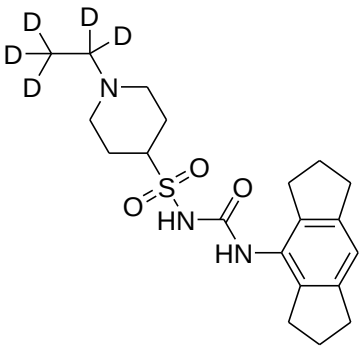
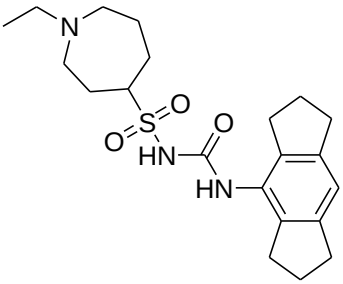
and .

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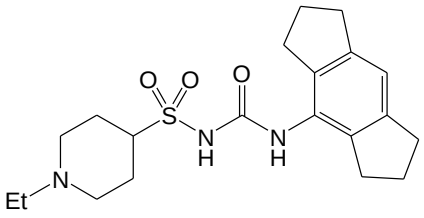
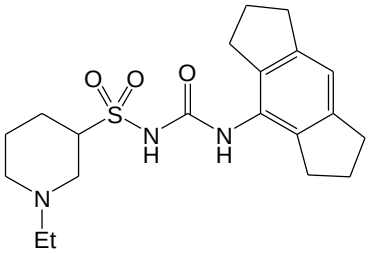
17. A compound selected from the group consisting of:



,

and pharmaceutically acceptable salts and solvates thereof.

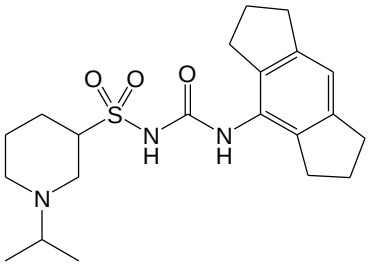
18. A compound selected from the group consisting of:



,

and pharmaceutically acceptable salts and solvates thereof.

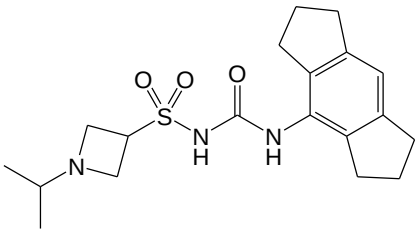
19. A compound selected from the group consisting of:



,

and pharmaceutically acceptable salts and solvates thereof.

20. A compound selected from the group consisting of:



,

and pharmaceutically acceptable salts and solvates thereof.

21. A pharmaceutically acceptable salt or solvate of a compound as claimed in any one of claims 1 to 20.

22. A pharmaceutical composition comprising a compound as claimed in any one of claims 1 to 20, or a pharmaceutically acceptable salt or solvate as claimed in claim 21, and a pharmaceutically acceptable excipient.

23. A compound as claimed in any one of claims 1 to 20, or a pharmaceutically acceptable salt or solvate as claimed in claim 21, or a pharmaceutical composition as claimed in claim 22, for use in medicine.

24. A compound, pharmaceutically acceptable salt, solvate, or pharmaceutical composition as claimed in claim 23, for use in the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is selected from:

(i) inflammation;
(ii) an auto-immune disease;
(iii) cancer;
(iv) an infection;
(v) a central nervous system disease;
(vi) a metabolic disease;
(vii) a cardiovascular disease;
(viii) a respiratory disease;
(ix) a liver disease;
(x) a renal disease;
(xi) an ocular disease;
(xii) a skin disease;
(xiii) a lymphatic condition;
(xiv) a psychological disorder;
(xv) graft versus host disease; and
(xvi) allodynia.

25. A compound, pharmaceutically acceptable salt, solvate, or pharmaceutical composition as claimed in claim 23, for use in the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is selected from:

(i) cryopyrin-associated periodic syndromes (CAPS);
(ii) Muckle-Wells syndrome (MWS);
(iii) familial cold autoinflammatory syndrome (FCAS);
(iv) neonatal onset multisystem inflammatory disease (NOMID);
(v) familial Mediterranean fever (FMF);

(vi) pyogenic arthritis, pyoderma gangrenosum and acne syndrome (PAPA);
(vii) hyperimmunoglobulinemia D and periodic fever syndrome (HIDS);
(viii) Tumour Necrosis Factor (TNF) Receptor-Associated Periodic Syndrome (TRAPS);
(ix) systemic juvenile idiopathic arthritis;
(x) adult-onset Still's disease (AOSD);
(xi) relapsing polychondritis;
(xii) Schnitzler's syndrome;
(xiii) Sweet's syndrome;
(xiv) Behcet's disease;
(xv) anti-synthetase syndrome;
(xvi) deficiency of interleukin 1 receptor antagonist (DIRA); and
(xvii) haploinsufficiency of A20 (HA20).

26. A compound as claimed in any one of claims 1 to 20, or a pharmaceutically acceptable salt or solvate as claimed in claim 21, or a pharmaceutical composition as claimed in claim 22, for use in inhibiting NLRP3.

27. Use of a compound as claimed in any one of claims 1 to 20, or a pharmaceutically acceptable salt or solvate as claimed in claim 21, or a pharmaceutical composition as claimed in claim 22, in the manufacture of a medicament for treating or preventing a disease, disorder or condition selected from:

(i) inflammation;
(ii) an auto-immune disease;
(iii) cancer;
(iv) an infection;
(v) a central nervous system disease;
(vi) a metabolic disease;
(vii) a cardiovascular disease;
(viii) a respiratory disease;
(ix) a liver disease;
(x) a renal disease;
(xi) an ocular disease;
(xii) a skin disease;
(xiii) a lymphatic condition;
(xiv) a psychological disorder;

(xv) graft versus host disease; and

(xvi) allodynia.

28. Use of a compound as claimed in any one of claims 1 to 20, or a pharmaceutically acceptable salt or solvate as claimed in claim 21, or a pharmaceutical composition as claimed in claim 22, in the manufacture of a medicament for treating or preventing a disease, disorder or condition selected from:

(i) cryopyrin-associated periodic syndromes (CAPS);

(ii) Muckle-Wells syndrome (MWS);

(iii) familial cold autoinflammatory syndrome (FCAS);

(iv) neonatal onset multisystem inflammatory disease (NOMID);

(v) familial Mediterranean fever (FMF);

(vi) pyogenic arthritis, pyoderma gangrenosum and acne syndrome (PAPA);

(vii) hyperimmunoglobulinemia D and periodic fever syndrome (HIDS);

(viii) Tumour Necrosis Factor (TNF) Receptor-Associated Periodic Syndrome (TRAPS);

(ix) systemic juvenile idiopathic arthritis;

(x) adult-onset Still's disease (AOSD);

(xi) relapsing polychondritis;

(xii) Schnitzler's syndrome;

(xiii) Sweet's syndrome;

(xiv) Behcet's disease;

(xv) anti-synthetase syndrome;

(xvi) deficiency of interleukin 1 receptor antagonist (DIRA); and

(xvii) haploinsufficiency of A20 (HA20).