Claims

1. A crystalline Form of an N-{3-[1-(2-nitrophenyl)-1H-pyrrol-2-yl]-allylidene}-aminoguanidinium salt selected from the group consisting of:

i. a crystalline Form A of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate exhibiting at least X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation at 11.5±0.2, 23.5±0.2, and 27.0±0.2,

ii. a crystalline Form B of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium succinate exhibiting at least X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation at 9.7±0.2, 22.8±0.2, and 26.7±0.2,

iii. a crystalline Form XIV of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium besylate exhibiting at least X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation at 13.0±0.2, 15.1±0.2, and 19.9±0.2,

iv. a crystalline Form XIX of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium oxoglutarate exhibiting at least X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation at 16.8±0.2, 23.4±0.2, and 23.6±0.2,

v. a crystalline Form XX of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium DL-mandelic acid exhibiting at least X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation at 14.8±0.2, 24.2±0.2, and 25.5±0.2,

vi. a crystalline Form XXII of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium hippuric acid exhibiting at least X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation at 20.1±0.2, 24.1±0.2, and 24.5±0.2,

vii. a crystalline Form XXIII of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium formate exhibiting at least X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation at 13.3±0.2, 15.1±0.2, and 25.6±0.2,

viii. a crystalline Form XXIV of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium L-lactic acid exhibiting at least X-ray lines (2-theta values) in

a powder diffraction pattern when measured using Cu K_α radiation at 3.8±0.2, 9.9±0.2, and 11.9±0.2,

ix. a crystalline Form XXV of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium DL-lactic acid exhibiting at least X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation at 9.8±0.2, 11.9±0.2, and 27.6±0.2,

x. a crystalline Form XXVI of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium glutaric acid exhibiting at least X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu Kα radiation at 8.3±0.2, 15.9±0.2, and 21.9±0.2, and

xi. a crystalline Form XXIX of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium adipic acid exhibiting at least X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation at 13.4±0.2, 14.5±0.2, and 25.5±0.2.

2. The crystalline Form A of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate according to claim 1 further exhibiting one or more X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation selected from the group consisting of 11.7±0.2, 13.0±0.2, 15.5±0.2, 15.6±0.2, 16.2±0.2, 19.6±0.2, 20.0±0.2, 21.1±0.2, and 24.8±0.2, optionally wherein the crystalline Form A is free of a second crystalline form of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate, wherein the second form exhibits X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation at 14.9±0.2, 18.0±0.2, and/or 24.2±0.2.

3. The crystalline Form A of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate according to any one of claims 1 and 2 exhibiting in differential scanning calorimetry an onset temperature between 185 and 199 °C using a heating rate of 10 °C per minute, such as 192 °C using a heating rate of 10 °C per minute.

4. The crystalline Form B of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium succinate according to claim 1 further exhibiting one or more X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu K_α radiation selected from the group consisting of 5.4±0.2, 12.2±0.2, 13.4±0.2, 15.8±0.2, 16.3±0.2, 19.5±0.2, 21.8±0.2, and 28.5±0.2.

5. The crystalline Form B of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium succinate according to any one of claims 1 and 4 exhibiting in differential scanning calorimetry an onset temperature between 187 and 201 °C using a heating rate of 10 °C per minute, such as 195 °C using a heating rate of 10 °C per minute.

6. A method for producing the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate of crystalline Form A according to any one of claims 1 to 3 or the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium succinate of crystalline Form B according to any one of claims 1 and 4 to 5, comprising:
    i. mixing *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidine and acetic acid in a solvent to form a mixture; and
    ii. isolating the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate of crystalline Form A from said mixture,

    or

    i. mixing a *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt and acetic acid in a solvent to form a mixture; and
    ii. isolating the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate of crystalline Form A from the mixture,

    or

    i. mixing *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate in a solvent to form a composition; and

ii. isolating the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate of crystalline Form A from said composition,

or

i. mixing 3-[1-(2-nitrophenyl)-1-*H*-pyrrole-2-yl]-propanal, amino guanidine or a salt thereof, and acetic acid or a salt thereof in a solvent, and
ii. isolating the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate of crystalline Form A from said composition,

or

i. providing *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidine or an *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt,
ii. introducing acetate as a counter ion using ion exchange, and
iii. isolating *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate of crystalline Form A,

or

i. mixing *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidine and succinic acid in a solvent to form a mixture; and
ii. isolating the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium succinate of crystalline Form B from the mixture,

or

i. mixing a *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt and succinic acid in a solvent to form a mixture, and
ii. isolating the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium succinate of crystalline Form B from the mixture,

or

i. mixing 3-[1-(2-nitrophenyl)-1-*H*-pyrrole-2-yl]-propanal, amino guanidine or a salt thereof, and succinic acid or a salt thereof in a solvent, and
ii. isolating the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium succinate of crystalline Form B from said composition,

or

i. providing *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidine or an *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt,
ii. introducing succinate as a counter ion using ion exchange, and
iii. isolating *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium succinate of crystalline Form B.

7. The crystalline Form A of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate according to any one of claims 1 to 3, the crystalline Form B of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium succinate according to any one of claims 1 and 4 to 5,
the crystalline Form XIV of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium besylate according to claim 1,
the crystalline Form XIX of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium oxoglutarate according to claim 1,
the crystalline Form XX of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium DL-mandelic acid according to claim 1,
the crystalline Form XXII of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium hippuric acid according to claim 1,
the crystalline Form XXIII of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium formate according to claim 1,
the crystalline Form XXIV of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium L-lactic acid according to claim 1,
the crystalline Form XXV of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-

aminoguanidinium DL-lactic acid according to claim 1,
the crystalline Form XXVI of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium glutaric acid according to claim 1, or
the crystalline Form XXIX of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium adipic acid according to claim 1,
for use in medicine.

8. Use of the crystalline Form A of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium acetate according to any one of claims 1 to 3, the crystalline Form B of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium succinate according to any one of claims 1 and 4 to 5,
the crystalline Form XIV of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium besylate according to claim 1,
the crystalline Form XIX of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium oxoglutarate according to claim 1,
the crystalline Form XX of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium DL-mandelic acid according to claim 1,
the crystalline Form XXII of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium hippuric acid according to claim 1,
the crystalline Form XXIII of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium formate according to claim 1,
the crystalline Form XXIV of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium L-lactic acid according to claim 1,
the crystalline Form XXV of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium DL-lactic acid according to claim 1,
the crystalline Form XXVI of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium glutaric acid according to claim 1, or
the crystalline Form XXIX of *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium adipic acid according to claim 1,
in the manufacture of a medicament for the treatment of a kidney disease, an arthritic disease, a cardiovascular disease, atherosclerosis, a viral disease or disorder, or a systemic inflammatory disorder, such as wherein the systemic inflammatory disorder is an autoimmune disorder or wherein the systemic inflammatory disorder is selected from the group consisting of Behçet disease, sarcoidosis, systemic lupus erythematosus, juvenile idiopathic arthritis,

scleroderma, Sjögren syndrome, myositis including dermamyositis and polymyositis, vasculitis, giant cell arteritis, ankylosing spondylitis, polymyalgia rheumatic and psoriatic arthritis.

9. The use according to claim 8, wherein the kidney disease is selected from the group consisting of:
    i. kidney disease presenting with proteinuria,
    ii. proteinuric kidney disease,
    iii. glomerular disease,
    iv. nephrotic syndrome (glomerulonephrosis),
    v. primary nephrotic syndrome (primary glomerulonephrosis), such as glomerulonephritis selected from the group consisting of IgA nephropathy (Berger's disease), IgM nephropathy, Post-infectious glomerulonephritis and thin basement membrane disease,
    vi. secondary nephrotic syndrome (secondary glomerulonephrosis), such as secondary nephrotic syndrome caused by an underlying autoimmune disease, an underlying cancer disease, an underlying genetic disorder, by an underlying disease selected from the group consisting of: Systemic lupus erythematosus (SLE), Diabetic nephropathy, Sarcoidosis, Sjögren's syndrome, Amyloidosis, Multiple myeloma, Vasculitis, Cancer and Genetic disorders (such as congenital nephrotic syndrome), by an infection, such as a urinary tract infection, such as an infection selected from the group consisting of HIV, syphilis, hepatitis such as hepatitis A, B and C, post-streptococcal infection, urinary schistosomiasis and Ebola,
    vii. an inflammatory kidney disease,
    viii. glomerulonephritis (GN), and
    ix. idiopathic membranous nephropathy (iMN).

10. The use according to claim 9, wherein said primary nephrotic syndrome is membranous glomerulonephritis (MGN) (or membranous nephropathy (MN)), focal segmental glomerulosclerosis (FSGS), membranoproliferative glomerulonephritis (MPGN) (mesangiocapillary glomerulonephritis) such as membranoproliferative glomerulonephritis (MPGN) is selected from Type 1

MPGN and Type 2 MPGN, rapidly progressive glomerulonephritis (RPGN) (crescentic GN), or minimal change disease (MCD).

11. The use according to claim 8, wherein the arthritic disease is selected from the group consisting of:
    i. an auto-immune disease and/or an inflammatory disease that presents with joint inflammation such as an inflammatory disease selected from the group consisting of systemic lupus erythematosus, mixed connective tissue disease, Still´s disease, and Polymyalgia Rheumatica,
    ii. inflammatory arthritis such as inflammatory arthritis selected from the group consisting of Rheumatoid Arthritis (RA) such as severe active RA (CDAI > 22) and/or RA with a DAS28 score of above 5.1, such as juvenile rheumatoid arthritis (JRA), Psoriatic Arthritis, and Ankylosing Spondylitis,
    iii. degenerative arthritis such as osteoarthritis,
    iv. metabolic arthritis such as gouty arthritis,
    v. reactive arthritis such as arthritis associated with infection with one or more of Hepatitis C, Chlamydia, gonorrhoea, salmonella or shigella,
    vi. infectious arthritis such as arthritis associated with infection with one or more of Hepatitis C, Chlamydia, gonorrhoea, salmonella or shigella, and
    vii. arthritis as part of a systemic inflammatory disease.

12. The use according to claim 8, wherein the viral disease or disorder is selected from the group consisting of:
    i. a symptomatic viral disease or disorder,
    ii. a symptomatic viral disease or disorder with inflammation,
    iii. an inflammatory viral disease or disorder,
    iv. a viral respiratory infection such as a viral lower respiratory infection,
    v. a viral respiratory disease or disorder,
    vi. a viral disease or disorder of the lung,
    vii. a viral disease or disorder with inflammation in the respiratory system such as a viral disease or disorder with inflammation in the respiratory system in the lungs and/or respiratory tract,

viii. a viral disease or disorder with one or more respiratory symptoms such as wherein said one or more respiratory symptoms are selected from the group consisting of cough, dry cough, dyspnea, impaired oxygenation, respiratory illness, respiratory dysfunction, respiratory failure, respiratory syndrome and acute respiratory disease (ARD),

ix. severe disease such as wherein said severe disease present with dyspnoea, increased respiratory frequency, reduced blood oxygen saturation and/or lung infiltrates,

x. critical disease such as wherein said critical disease present with respiratory failure, septic shock, and/or multiple organ dysfunction (MOD) or multiple organ failure (MOF),

xi. viral pneumonia,

xii. viral bronchiolitis,

xiii. viral diseases or disorders with respiratory failure,

xiv. acute respiratory distress syndrome (ARDS),

xv. viral acute respiratory distress syndrome (ARDS),

xvi. symptomatic COVID-19 with acute respiratory distress syndrome (ARDS),

xvii. a viral disease or disorder with systemic inflammatory distress syndrome (SIDS) and/or sepsis,

xviii. a viral disease or disorder with pulmonary insufficiency,

xix. a viral disease or disorder with cytokine release syndrome (CRS) and/or a cytokine storm (hypercytokinemia), and

xx. a viral disease or disorder caused by a viral infection selected from the group consisting of Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2); SARS-CoV, MERS-CoV, the dengue virus and influenza virus (including Type A, Type B and Type C), such as wherein the inflammation is hyperinflammation, such as hyperinflammation in one or more organs, such as wherein the one or more organs is selected from the group consisting of lungs, the respiratory tract, kidney, liver, pancreas, spleen, exocrine glands, endocrine glands, lymph nodes, brain, heart, muscles, bone marrow, skin, skeleton, bladder, reproduction organs including the phallopian tubes, eye, ear, vascular system, the gastroinstestinal tract including small intestines, colon, rectum, canalis analis and the prostate gland.

13. The use according to claim 8, wherein the cardiovascular disease is selected from the group consisting of:

i. coronary artery diseases (CAD) such as wherein the coronary artery diseases (CAD) is selected from the group consisting of angina and myocardial infarction,
ii. stroke,
iii. heart failure,
iv. hypertensive heart disease,
v. rheumatic heart disease,
vi. cardiomyopathy,
vii. abnormal heart rhythms,
viii. congenital heart disease,
ix. valvular heart disease,
x. carditis,
xi. aortic aneurysms,
xii. peripheral artery disease,
xiii. vascular disease,
xiv. thromboembolic disease,
xv. venous thrombosis,
xvi. vascular inflammation, and
xvii. atherosclerotic cardiovascular disease such as wherein the atherosclerotic cardiovascular disease is selected from the group consisting of coronary artery disease, stroke (cerebrovascular disease), and peripheral artery disease.

14. The use according to claim 11, wherein the treatment is treatment of rheumatoid arthritis in a subject with an inappropriate response to MTX, such as wherein the inappropriate response to MTX is reduced response to MTX treatment, such as an MTX non-responder.

15. A method for producing the crystalline Form of the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt according to claim 1, comprising:

i. mixing *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidine and an acid in a solvent to form a mixture; and

ii. isolating the crystalline Form of the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt from said mixture,

or

i. mixing a second *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt and an acid in a solvent to form a mixture; and

ii. isolating the crystalline Form of the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt from the mixture,

or

i. mixing an amorphous form or a second crystalline form *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt in a solvent to form a composition; and

ii. isolating the crystalline Form of the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt from said composition,

or

i. mixing 3-[1-(2-nitrophenyl)-1-*H*-pyrrole-2-yl]-propanal, amino guanidine or a salt thereof, and an acid or a salt thereof in a solvent, and

ii. isolating the crystalline form of the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt from said composition,

or

i. providing *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidine or an second *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt,

ii. introducing a counter ion of an acid ion using ion exchange, and

iii. isolating the crystalline Form of the *N*-{3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-allylidene}-aminoguanidinium salt.

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