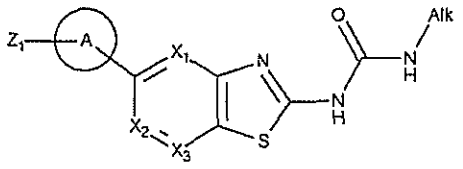
CLAIMS:

1. A method for the treatment or prevention of a bacterial infection comprising administration of a bacterial type II topoisomerase inhibitor in combination with a polymyxin or polymyxin derivative to a subject suffering from infection or at risk of infection, wherein the bacterial infection is caused by a Gram-negative bacteria or drug resistant Gram-negative bacteria and the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and optionally on-target enzyme activity against topoisomerase IV.

2. The method according to claim 1 wherein the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and on-target enzyme activity against topoisomerase IV.

3. The method according to claim 1 or claim 2 wherein the bacterial type II topoisomerase inhibitor is a GyrB/ParE inhibitor.

4. The method according to any one of claims 1 to 3 wherein the bacterial type II topoisomerase inhibitor is a compound of Formula (I):



Formula (I)

and; salts, racemates, diastereomers, enantiomers, deuterated forms, hydrates, solvates and prodrugs thereof

wherein:

Alk is an optionally substituted C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, or C_{3-6}cycloalkyl;

A represents "Ring A" which is selected from saturated or unsaturated monocyclic C_{3-7}cycloalkyl, saturated or unsaturated monocyclic 3-7 membered heterocyclyl, saturated or unsaturated fused bicyclic C_{8-10}cycloalkyl, saturated or unsaturated fused bicyclic 8-10 membered-heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl and may be optionally substituted;

X_1 is CH, -N= or C-R_1, where R_1 is selected from OH, optionally substituted C_{1-3}alkyl, optionally substituted C_{2-3}alkenyl, optionally substituted C_{2-3}alkynyl, optionally substituted C_{1-3}alkoxyl, halo, haloC_{1-3}alkyl, NH_2, optionally substituted NHC_{1-3}alkyl, optionally substituted $N(C_{1-3}alkyl)_2$, optionally substituted SC_{1-3}alkyl and CN;

X_2 is CH, -N= or C-R_2, where R_2 is selected from OH, optionally substituted C_{1-6}alkyl, optionally substituted C_{2-6}alkenyl, optionally substituted C_{2-6}alkynyl, optionally substituted $(CH_2)_mOC_{1-6}$alkyl, optionally substituted $(CH_2)_mSC_{1-6}$alkyl, optionally substituted $(CH_2)_mS(=O)C_{1-6}$alkyl, optionally substituted $(CH_2)_mO(CH_2)_mC_{3-7}$cycloalkyl, optionally

substituted $(CH_2)_mC_{3-7}$cycloalkyl, optionally substituted $(CH_2)_mO(CH_2)_m$phenyl, optionally substituted $(CH_2)_m$phenyl, optionally substituted $(CH_2)_mO(CH_2)_m$-5-10-membered heterocycle, optionally substituted $(CH_2)_m$-5-10-membered heterocyclyl, halo, optionally substituted haloC_{1-3}alkyl, CN and optionally substituted $(CH_2)_mNR^aR^b$;

X_3 is CH, -N= or C-R_3, where R_3 is selected from OH, optionally substituted C_{1-6}alkyl, optionally substituted C_{2-6}alkenyl, optionally substituted C_{2-6}alkynyl, optionally substituted $(CH_2)_mOC_{1-6}$alkyl, optionally substituted $(CH_2)_mSC_{1-6}$alkyl, optionally substituted $(CH_2)_mS(=O)C_{1-6}$alkyl, optionally substituted $(CH_2)_mO(CH_2)_mC_{3-7}$cycloalkyl, optionally substituted $(CH_2)_mC_{3-7}$cycloalkyl, optionally substituted $(CH_2)_mO(CH_2)_m$phenyl, optionally substituted $(CH_2)_m$phenyl, optionally substituted $(CH_2)_mO(CH_2)_m$-5-10-membered heterocycle, optionally substituted $(CH_2)_m$-5-10-membered heterocyclyl, halo, optionally substituted haloC_{1-3}alkyl, CN and optionally substituted $(CH_2)_mNR^aR^b$;

each R^a and R^b is independently selected from H, optionally substituted C_{1-6}alkyl, optionally substituted C_{3-6}cycloalkyl and optionally substituted 4-6-membered heterocyclyl or R^a and R^b join together to form an optionally substituted 4-6-membered heterocyclyl;

each m is an integer independently selected from 0, 1, 2 and 3;

Z_1 is selected from H, halo, C_{1-6}alkyl, a 5-membered heterocyclic ring, a 6-membered heterocyclic ring, OH, OC_{1-6}alkyl, C_{1-6}alkoxyl, cyano (CN), a carbonyl moiety (=O), $C(=O)OC_{1-6}$alkyl, NH_2, NH-C_{1-6}alkyl, N(C_{1-6}alkyl)$_2$, and C(=O)NH-C_{1-6}alkyl;

or Z_1 is a carbonyl containing group of general formula $-(Y)_qB(R_4)$-C(=O)-W-R_5 wherein:

q is an integer 0 or 1;

Y is attached to Ring A and when q is 0 then Y is a covalent bond, a spiro ring centre, or a fused ring bond; or when q is 1 then Y is selected from optionally substituted C_{1-3}alkylene, optionally substituted C_{2-3}alkenylene and optionally substituted C_{2-3}alkynylene and wherein each carbon atom in C_{1-3}alkylene may be optionally replaced by an oxygen or nitrogen heteroatom or C(=O);

B represents "Ring B" and is selected from saturated or unsaturated monocyclic C_{3-7}cycloalkyl, saturated or unsaturated monocyclic 3-7 membered heterocycle, saturated or unsaturated fused bicyclic C_{8-10}cycloalkyl, saturated or unsaturated fused bicyclic 8-12 membered heterocyclyl, C_{6-10}aryl, 5-10 membered heteroaryl, and a spiro bicyclic 8-12 membered heterocyclic ring system; and further Ring B may be optionally substituted; or Ring B may join together with Ring A to form a saturated or unsaturated fused bicyclic C_{8-10}cycloalkyl,a saturated or unsaturated fused bicyclic 8-10 membered heterocyclyl and a spiro bicyclic 8-12 membered heterocyclic ring system;

R_4 is joined to the same Ring B atom as the -C(=O)-W-R_5 moiety and is selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, (C_{1-6}alkyl)$_t$$C_{3-7}$cycloalkyl, ($C_{1-6}$alkyl)$_t$aryl, ($C_{1-6}$alkyl)$_t$heterocyclyl, ($C_{1-6}$alkyl)$_t$heteroaryl, NH_2, NH(C_{1-6}alkyl), N(C_{1-6}alkyl)$_2$, CN, OH,

C_{1-6}alkoxy, SO_2H, SO_2C_{1-6}alkyl, SH, SC_{1-6}alkyl, halo, haloC_{1-6}alkyl, -NH(C=O)OC_{1-6}alkyl, -NH(C=O)OC(C_{1-3}alkyl)$_3$, and wherein C_{1-3}alkyl, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-7}cycloalkyl, aryl and heterocyclyl in each case may be further optionally substituted or R_4 is a chain of 3 or 4 carbon atoms or carbon and heteroatoms which joins with an adjacent B ring atom to form a fused carbocyclylic or heterocycylic ring which is optionally further substituted;

the -C(=O)-W-R_5 moiety is joined to the same Ring B atom as R_4 wherein:

W is O, NH or N(C_{1-6}alkyl);

R_5 is selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, $S(O)_2OH$, $S(O)_2$-C_{1-6}alkyl, or M where M represents a monovalent or divalent cation selected from the group comprising pharmaceutically acceptable cations, such as sodium, potassium, lithium, calcium, magnesium, zinc, ammonium, alkylammonium such as salts formed from triethylamine, alkoxyammonium such as those formed with ethanolamine and salts formed from ethylenediamine, choline or amino acids;

or Z_1 is an alcohol containing group of general formula $(CH_2)_sC(OH)(R_6)(R_7)$ or an ester, carbamate, phosphate, sulfate or prodrug thereof wherein the OH, R_6 and R_7 groups are each attached to the same carbon atom; and

wherein:

s is an integer selected from 0, 1, 2 and 3;

R_6 is H or is selected from optionally substituted C_{1-6}alkyl, optionally substituted C_{2-6}alkenyl, optionally substituted C_{2-6}alkynyl, optionally substituted $(CH_2)_tOC_{1-6}$alkyl, optionally substituted $(CH_2)_tOC(=O)C_{1-6}$alkyl, optionally substituted $(CH_2)_tSC_{1-6}$alkyl, optionally substituted $(CH_2)_tS(=O)C_{1-6}$alkyl, halo, optionally substituted haloC_{1-3}alkyl and optionally substituted $(CH_2)_tNR^aR^b$;

R_7 is selected from optionally substituted C_{1-6}alkyl, optionally substituted C_{2-6}alkenyl, optionally substituted C_{2-6}alkynyl, optionally substituted C_{3-7}cycloalkyl ring, optionally substituted phenyl, optionally substituted 4-6-membered heterocyclyl ring, optionally substituted 5-6-membered heteroaryl ring, optionally substituted $(CH_2)_tOC_{1-6}$alkyl, optionally substituted $(CH_2)_tOC(=O)C_{1-6}$alkyl, optionally substituted $(CH_2)_tSC_{1-6}$alkyl, optionally substituted $(CH_2)_tS(=O)C_{1-6}$alkyl, halo, optionally substituted haloC_{1-3}alkyl and optionally substituted $(CH_2)_tNR^aR^b$;

t is an integer selected from 1, 2, 3, 4, 5 and 6;

or R_6 and R_7 together with the carbon atom to which they are attached form an optionally substituted 4-6-membered heterocyclic ring or C_{3-7}cycloalkyl ring;

and further wherein the prodrug is selected from an ester, carbamate, phosphate or sulfate formed from the hydroxyl moiety;

or Z_1 a sulfonamide containing group of general formula $(CH_2)_vNRS(=O)_2R_8$ or $(CH_2)_vS(=O)_2NR_9R_{10}$ or a sulfamide containing group of general formula

$(CH_2)_vNRS(=O)_2NR_9R_{10}$ wherein:

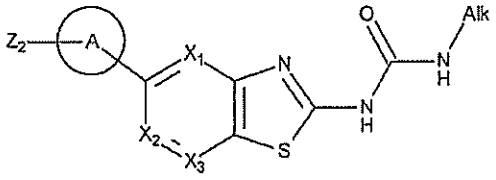
v is an integer 0, 1, 2 or 3;

R is H or an optionally substituted C_{1-6}alkyl; and

R_8, R_9 and R_{10} are each independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-7}cycloalkyl, phenyl, benzyl, a 3-10-membered heterocyclic ring, a 5-10-membered heteroaryl ring and further wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-7}cycloalkyl, phenyl, benzyl, a 3-10-membered heterocyclic ring, a 5-10-membered heteroaryl ring may be optionally substituted;

or R_9 and R_{10} may join to form an optionally substituted 3-6-membered heterocyclic ring together with the nitrogen to which they are attached.

5. The method according to any one of claims 1 to 3 wherein the bacterial type II topoisomerase inhibitor is a compound of Formula (II):



Formula (II)

and; salts, racemates, diastereomers, enantiomers, deuterated forms, hydrates, solvates and prodrugs thereof:

wherein Alk, Ring A, X_1, X_2 and X_3 are according to claim 4; and

Z_2 is $(CH_2)_vNRS(=O)_2R_8$, $(CH_2)_vS(=O)_2NR_9R_{10}$ or $(CH_2)_vNRS(=O)_2NR_9R_{10}$;

wherein

v is an integer 0, 1, 2 or 3;

R is H or an optionally substituted C_{1-6}alkyl; and

R_8, R_9 and R_{10} are each independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-7}cycloalkyl, phenyl, benzyl, a 3-10-membered heterocyclic ring, or a 5-10-membered heteroaryl ring and further wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-7}cycloalkyl, phenyl, benzyl, 3-10-membered heterocyclic ring and 5-10-membered heteroaryl ring may be optionally substituted;

or R_9 and R_{10} may join to form an optionally substituted 3-6-membered heterocyclic ring together with the nitrogen to which they are attached.

6. The method according to any one of claims 1 to 5 wherein the polymyxin and polymyxin derivative is selected from an antibacterial polymyxin, an antibacterial polymyxin derivative, a non-antibacterial polymyxin, and a non-antibacterial polymyxin derivative.

7. The method according to any one of claims 1 to 6 wherein the polymyxin is Polymyxin B (PMB) or colistin (Polymyxin E).

8. The method according to any one of claims 1 to 6 wherein the polymyxin derivative is Polymyxin B nonapeptide (PMBN) or a prodrug of colistin.

9. The method according to any one of claims 1 to 8 wherein the polymyxin or polymyxin derivative is provided in a therapeutically effective antibacterial amount or dosage.

10. The method according to any one of claims 1 to 8 wherein the polymyxin or polymyxin derivative is provided in a sub-inhibitory antibacterial MIC amount or dosage.

11. The method according to any one of claims 1 to 10 wherein the combination may be administered concurrently, sequentially or separately to a patient suffering from infection or at risk of infection.

12. The method according to any one of claims 1 to 11 wherein the Gram-negative bacteria or drug resistant Gram-negative bacteria comprises a lipopolysaccharide (LPS) layer.

13. The method according to any one of claims 1 to 11 wherein the Gram-negative bacteria or drug resistant Gram-negative bacteria comprises a lipooligosaccharide (LOS) layer.

14. The method according to any one of claims 1 to 11 wherein the Gram-negative bacteria is one or more bacterial strains selected from the group comprising *E. coli*, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa*, and *Enterobacter spp* and drug resistant strains thereof.

15. The method according to any one of claims 1 to 11 wherein the Gram-negative pathogen is one or more bacterial strains selected from the group comprising *M. catarrhalis*, *Neisseria*, *Haemophilus* and *Bordetella* and drug resistant strains thereof.

16. The method according to any one of claims 1 to 11 wherein the Gram-negative pathogen is one or more bacterial strains selected from the group comprising *L. pneumoniae*, *C. trachomatis*, *C. pneumonia*, *Y. pestis*, *F. tularensis*, *B.pseudomallei*, *C. burnetii*, *Brucella* species, *B. mallei*, *C. psittaci* and *R. prowazekii*.

17. The method according to any one of claims 1 to 11 wherein the subject is suffering from or at risk of an intra-abdominal infection (IAI), hospital acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), urinary tract infection (UTI), bacteremias, community acquired bacterial pneumonia (CABP), gonococcal infection (GI), wound or surgical site infections, endocarditis, otitis media, cystic fibrosis or meningitis.

18. Use of a bacterial type II topoisomerase inhibitor in combination with a polymyxin or polymyxin derivative in the treatment or prevention of a bacterial infection wherein the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and optionally on-target enzyme activity against topoisomerase IV and wherein the bacterial infection is caused by a Gram-negative bacteria or drug resistant Gram-negative bacteria.

19. Use of a bacterial type II topoisomerase inhibitor in combination with a polymyxin or polymyxin derivative in the preparation of a medicament for the treatment or prevention of a bacterial infection wherein the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and optionally on-target enzyme activity against topoisomerase IV

and wherein the bacterial infection is caused by a Gram-negative bacteria or drug resistant Gram-negative bacteria.

20. A method of improving the antibacterial activity of a bacterial type II topoisomerase inhibitor wherein the method comprises the step of administration of a bacterial type II topoisomerase inhibitor with a polymyxin or polymyxin derivative to a subject suffering from a bacterial infection or at risk of a bacterial infection wherein the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and optionally on-target enzyme activity against topoisomerase IV and wherein the bacterial infection is caused by a Gram-negative bacteria or drug resistant Gram-negative bacteria.

21. A method of improving the antibacterial efficacy of a bacterial type II topoisomerase inhibitor wherein the method comprises the step of administration of a bacterial type II topoisomerase inhibitor with a polymyxin or polymyxin derivative to a subject suffering from a bacterial infection or at risk of a bacterial infection wherein the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and optionally on-target enzyme activity against topoisomerase IV and wherein the bacterial infection is caused by a Gram-negative bacteria or drug resistant Gram-negative bacteria.

22. A composition comprising a bacterial type II topoisomerase inhibitor and a polymyxin or polymyxin derivative wherein the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and optionally on-target enzyme activity against topoisomerase IV.

23. An antibacterial agent comprising a bacterial type II topoisomerase inhibitor and a polymyxin or polymyxin derivative wherein the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and optionally on-target enzyme activity against topoisomerase IV.

24. A compound of Formula (II) as defined in Claim 5 or a salt, racemate, diastereomer, enantiomer, ester, carbamate, phosphate, sulfate, deuterated form or prodrug thereof.

25. A process for the manufacture of a compound of Formula (II) as defined in Claim 24 or a salt, racemate, diastereomer, enantiomer, ester, carbamate, phosphate, sulfate, deuterated form or prodrug thereof.

26. A compound of selected from the group consisting of:

A-10) 2-[[5-[2-(Ethylcarbamoylamino)-7-(2-pyridyl)-1,3-benzothiazol-5-yl]pyrimidin-2-yl]sulfamoyl]benzoic acid;

A-11) 1-Ethyl-3-[7-(5-methyl-2-pyridyl)-5-[2-(pyrrolidin-1-ylsulfonylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]urea;

A-12) 1-Ethyl-3-[7-(5-methyl-2-pyridyl)-5-[2-(propylsulfonylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]urea;

A-13) 1-[5-[2-(tert-Butylsulfonylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-14) 1-Ethyl-3-[5-[2-[(2-hydroxy-1,1-dimethyl-ethyl)sulfonylamino]pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-15) 1-Ethyl-3-[5-[2-[[2-hydroxyethyl(methyl)sulfamoyl]amino]pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-16) Methyl 2-[[5-[2-(ethylcarbamoylamino)-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-5-yl]pyrimidin-2-yl]sulfamoyl]acetate;

A-17) 1-[5-[2-(allylsulfonylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-18) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-[2-(dimethylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-19) 1-ethyl-3-[5-[2-(methanesulfonamidomethyl)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-20) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-[4-(2-pyrrolidin-1-ylethyl)piperazin-1-yl]-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-21) 1-[5-[2-(cyclopentylsulfonylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-24) 1-(5-(2-(1,1-dioxido-1,2-thiazinan-2-yl)pyrimidin-5-yl)-7-(pyridin-2-yl)benzo[d]thiazol-2-yl)-3-ethylurea;

A-25) 1-[5-[6-(1,1-dioxo-1,2-thiazolidin-2-yl)-3-pyridyl]-7-(2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethylurea;

A-26) 1-(5-(2-(1,1-dioxidoisothiazolidin-2-yl)pyrimidin-5-yl)-7-(pyridin-2-yl)benzo[d]thiazol-2-yl)-3-ethylurea;

A-27) 1-(5-(2-(1,1-dioxidoisothiazolidin-2-yl)pyrimidin-5-yl)-6-((tetrahydrofuran-2-yl)methoxy)benzo[d]thiazol-2-yl)-3-ethylurea;

A-28) 1-(5-(2-(1,1-dioxidoisothiazolidin-2-yl)pyrimidin-5-yl)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-2-yl)-3-ethylurea;

A-29) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-N-methylmethanesulfonamide;

A-30) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)methanesulfonamide;

A-31) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)methanesulfonamide;

A-32) 1-[5-[2-(dimethylsulfamoylamino)pyrimidin-5-yl]-7-(2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl urea;

A-33) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)propane-1-sulfonamide;

A-34) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)cyclopropanesulfonamide;

A-35) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)cyclopentanesulfonamide;

A-36) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)ethanesulfonamide;

A-37) 1-ethyl-3-[5-[2-(ethylsulfamoylamino)pyrimidin-5-yl]-7-(2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-38) 1-[5-[2-(dimethylsulfamoylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl urea;

A-39) 1-ethyl-3-[5-[2-(ethylsulfamoylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-40) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)cyclopropanesulfonamide;

A-41) 1-ethyl-3-[5-[2-(methylsulfamoylamino)pyrimidin-5-yl]-7-(2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-42) 1-ethyl-3-[7-(5-methyl-2-pyridyl)-5-[2-(methylsulfamoylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]urea;

A-43) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)morpholine-4-sulfonamide;

A-44) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)morpholine-4-sulfonamide;

A-45) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)pyrrolidine-1-sulfonamide;

A-46) (S)-2-amino-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-phenylpropane-1-sulfonamide;

A-47) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)ethanesulfonamide;

A-48) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)propane-2-sulfonamide;

A-49) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-methoxyazetidine-1-sulfonamide;

A-50) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-methoxyazetidine-1-sulfonamide;

A-51) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)benzenesulfonamide;

A-52) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-morpholinoethanesulfonamide;

A-53) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)pyrrolidine-3-sulfonamide;

A-54) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-hydroxypyrrolidine-1-sulfonamide;

A-55) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-1-(hydroxymethyl)cyclopropane-1-sulfonamide;

A-56) (R)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-morpholinopyrrolidine-1-sulfonamide;

A-57) (R)-3-(dimethylamino)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)pyrrolidine-1-sulfonamide;

A-58) 1-acetyl-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)pyrrolidine-3-sulfonamide;

A-59) (R)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-hydroxypyrrolidine-1-sulfonamide;

A-60) (S)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-hydroxypyrrolidine-1-sulfonamide;

A-61) N-(5-(2-(3-ethylureido)-6-fluorobenzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-62) (R)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-(hydroxymethyl)pyrrolidine-1-sulfonamide;

A-63) (S)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)tetrahydrofuran-3-sulfonamide;

A-64) N-(5-(7-bromo-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-65) 1-[7-bromo-5-[6-(tert-butylsulfonylamino)-3-pyridyl]-1,3-benzothiazol-2-yl]-3-ethyl urea;

A-66) methyl 2-[[5-[2-(ethylcarbamoylamino)-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-5-yl]pyrimidin-2-yl]sulfamoyl]acetate;

A-67) (R)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-1-(tetrahydro-2H-pyran-2-yl)methanesulfonamide;

A-68) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methoxyethanesulfonamide;

A-69) 1-[5-[6-(tert-butylsulfonylamino)-3-pyridyl]-7-(2-ethylthiazol-4-yl)-1,3-benzothiazol-2-yl]-3-ethyl urea;

A-70) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-hydroxyethanesulfonamide;

A-71) N-(5-(2-(3-ethylureido)-7-(1H-pyrazol-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-72) N-(5-(7-(3,5-dimethylisoxazol-4-yl)-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-73) N-(5-(2-(3-ethylureido)-7-(1-methyl-1H-pyrazol-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-74) N-(5-(2-(3-ethylureido)-7-((5-methylpyridin-2-yl)amino)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-75) N-(5-(2-(3-ethylureido)-7-methylbenzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-76) N-(5-(2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-77) N-(5-(7-cyclopropyl-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-78) N-(5-(2-(3-ethylureido)-7-(tetrahydro-2H-pyran-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-79) N-(5-(2-(3-ethylureido)-7-(pyrrolidin-1-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-80) N-(5-(2-(3-ethylureido)-7-(piperazin-1-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-81) N-(5-(2-(3-ethylureido)-7-morpholinobenzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-82) N-(5-(2-(3-ethylureido)-7-(4-methylpiperazin-1-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-83) N-(5-(7-(4-acetylpiperazin-1-yl)-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-84) N-(5-(2-(3-ethylureido)-7-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-85) N-(5-(2-(3-ethylureido)-7-(4-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-86) N-(5-(2-(3-ethylureido)-7-(5-(morpholinomethyl)pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-87) N-(5-(2-(3-ethylureido)-7-(2-(3-hydroxypyrrolidin-1-yl)thiazol-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-88) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-(2-hydroxy-4-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-89) N-(5-(2-(3-ethylureido)-7-(1-methyl-2-oxo-1,2-dihydropyridin-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-90) 2-(4-(5-(2-(1,1-dimethylethylsulfonamido)pyrimidin-5-yl)-2-(3-ethylureido)benzo[d]thiazol-7-yl)piperazin-1-yl)-N-methylacetamide;

A-91) ethyl 2-(4-(5-(2-(1,1-dimethylethylsulfonamido)pyrimidin-5-yl)-2-(3-ethylureido)benzo[d]thiazol-7-yl)piperazin-1-yl)acetate;

A-92) N-(5-(2-(3-ethylureido)-7-(2-(piperazin-1-yl)thiazol-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-93) N-(5-(2-(3-ethylureido)-7-(6-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-94) N-(5-(7-(2-aminopyridin-3-yl)-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-95) N-(5-(7-(5-aminopyridin-3-yl)-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-96) N-(5-(2-(3-ethylureido)-7-(4-(2-methoxyethyl)piperazin-1-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-97) N-(5-(2-(3-ethylureido)-7-(piperidin-1-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-98) N-(5-(7-(5-(aminomethyl)-2-fluorophenyl)-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-99) N-(5-(2-(3-ethylureido)-7-[2-dimethylaminoethyl(methyl)amino]benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-100) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-103) 1-[6-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-5-methoxy-thiazolo[5,4-b]pyridin-2-yl]-3-ethylurea;

A-104) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-(5-hydroxy-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethylurea;

A-105) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-[4-[(cyclopropylamino)methyl]-2-pyridyl]-1,3-benzothiazol-2-yl]-3-ethylurea;

A-106) 1-[7-(5-amino-2-pyridyl)-5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]-3-ethylurea;

A-107) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-(3-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-110) 1-[7-(4-amino-2-pyridyl)-5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]-3-ethylurea;

A-111) 1-[5-[2-(2,3-dihydroxypropylsulfonylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethylurea;

A-113) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-(4,5-dimethyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethylurea;

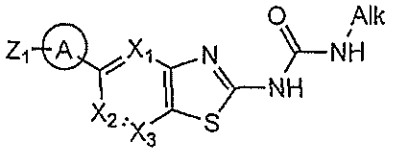
A-114) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-[(3S,4R,5R,6R)-3,4,5,6-tetrahydroxycyclohexen-1-yl]-1,3-benzothiazol-2-yl]-3-ethylurea; and

A-115) 1-[7-[(3aR,6aR)-2,3,3a,4,6,6a-hexahydro-1H-pyrrolo[2,3-c]pyrrol-5-yl]-5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]-3-ethyl-urea; or

a salt, racemate, diastereomer, enantiomer, ester, carbamate, phosphate, sulfate, deuterated form or prodrug thereof.

CLAIMS

1. The use of a compound of Formula (I):



Formula (I) and; salts, racemates, diastereomers, enantiomers, deuterated forms, hydrates, solvates and prodrugs thereof in combination with a polymyxin or polymyxin derivative for treatment of a bacterial infection in a subject caused by a Gram negative bacteria or a drug resistant Gram negative bacteria

wherein:

Alk is an optionally substituted C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, or C_{3-6}cycloalkyl;

A represents "Ring A" which is selected from saturated or unsaturated monocyclic C_{3-7}cycloalkyl, saturated or unsaturated monocyclic 3-7 membered heterocyclyl, saturated or unsaturated fused bicyclic C_{8-10}cycloalkyl, saturated or unsaturated fused bicyclic 8-10 membered-heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl and may be optionally substituted;

X_1 is CH, -N= or C-R_1, where R_1 is selected from OH, optionally substituted C_{1-3}alkyl, optionally substituted C_{2-3}alkenyl, optionally substituted C_{2-3}alkynyl, optionally substituted C_{1-3}alkoxyl, halo, haloC_{1-3}alkyl, NH_2, optionally substituted NHC_{1-3}alkyl, optionally substituted $N(C_{1-3}alkyl)_2$, optionally substituted SC_{1-3}alkyl and CN;

X_2 is CH, -N= or C-R_2, where R_2 is selected from OH, optionally substituted C_{1-6}alkyl, optionally substituted C_{2-6}alkenyl, optionally substituted C_{2-6}alkynyl, optionally substituted $(CH_2)_mOC_{1-6}$alkyl, optionally substituted $(CH_2)_mSC_{1-6}$alkyl, optionally substituted $(CH_2)_mS(=O)C_{1-6}$alkyl, optionally substituted $(CH_2)_mO(CH_2)_mC_{3-7}$cycloalkyl, optionally substituted $(CH_2)_mC_{3-7}$cycloalkyl, optionally substituted $(CH_2)_mO(CH_2)_m$phenyl, optionally substituted $(CH_2)_m$phenyl, optionally substituted $(CH_2)_mO(CH_2)_m$-5-10-membered heterocycle, optionally substituted $(CH_2)_m$-5-10-membered heterocyclyl, halo, optionally substituted haloC_{1-3}alkyl, CN and optionally substituted $(CH_2)_mNR^aR^b$;

X_3 is CH, -N= or C-R_3, where R_3 is selected from OH, optionally substituted C_{1-6}alkyl, optionally substituted C_{2-6}alkenyl, optionally substituted C_{2-6}alkynyl, optionally substituted $(CH_2)_mOC_{1-6}$alkyl, optionally substituted $(CH_2)_mSC_{1-6}$alkyl, optionally substituted $(CH_2)_mS(=O)C_{1-6}$alkyl, optionally substituted $(CH_2)_mO(CH_2)_mC_{3-7}$cycloalkyl, optionally substituted $(CH_2)_mC_{3-7}$cycloalkyl, optionally substituted $(CH_2)_mO(CH_2)_m$phenyl, optionally substituted $(CH_2)_m$phenyl, optionally substituted $(CH_2)_mO(CH_2)_m$-5-10-membered heterocycle,

optionally substituted $(CH_2)_m$-5-10-membered heterocyclyl, halo, optionally substituted haloC_{1-3}alkyl, CN and optionally substituted $(CH_2)_mNR^aR^b$;

each R^a and R^b is independently selected from H, optionally substituted C_{1-6}alkyl, optionally substituted C_{3-6}cycloalkyl and optionally substituted 4-6-membered heterocyclyl or R^a and R^b join together to form an optionally substituted 4-6-membered heterocyclyl;

each m is an integer independently selected from 0, 1, 2 and 3;

Z_1 is selected from H, halo, C_{1-6}alkyl, a 5-membered heterocyclic ring, a 6-membered heterocyclic ring, OH, OC_{1-6}alkyl, C_{1-6}alkoxyl, cyano (CN), a carbonyl moiety (=O), $C(=O)OC_{1-6}$alkyl, NH_2, NH-C_{1-6}alkyl, $N(C_{1-6}alkyl)_2$, and C(=O)NH-C_{1-6}alkyl;

or Z_1 is a carbonyl containing group of general formula $-(Y)_qB(R_4)$-C(=O)-W-R_5 wherein:

q is an integer 0 or 1;

Y is attached to Ring A and when q is 0 then Y is a covalent bond, a spiro ring centre, or a fused ring bond; or when q is 1 then Y is selected from optionally substituted C_{1-3}alkylene, optionally substituted C_{2-3}alkenylene and optionally substituted C_{2-3}alkynylene and wherein each carbon atom in C_{1-3}alkylene may be optionally replaced by an oxygen or nitrogen heteroatom or C(=O);

B represents "Ring B" and is selected from saturated or unsaturated monocyclic C_{3-7}cycloalkyl, saturated or unsaturated monocyclic 3-7 membered heterocycle, saturated or unsaturated fused bicyclic C_{8-10}cycloalkyl, saturated or unsaturated fused bicyclic 8-12 membered heterocyclyl, C_{6-10}aryl, 5-10 membered heteroaryl, and a spiro bicyclic 8-12 membered heterocyclic ring system; and further Ring B may be optionally substituted; or Ring B may join together with Ring A to form a saturated or unsaturated fused bicyclic C_{8-10}cycloalkyl,a saturated or unsaturated fused bicyclic 8-10 membered heterocyclyl and a spiro bicyclic 8-12 membered heterocyclic ring system;

R_4 is joined to the same Ring B atom as the -C(=O)-W-R_5 moiety and is selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, $(C_{1-6}alkyl)_tC_{3-7}$cycloalkyl, $(C_{1-6}alkyl)_t$aryl, $(C_{1-6}alkyl)_t$heterocyclyl, $(C_{1-6}alkyl)_t$heteroaryl, NH_2, NH(C_{1-6}alkyl), N(C_{1-6}alkyl)$_2$, CN, OH, C_{1-6}alkoxy, SO_2H, SO_2C_{1-6}alkyl, SH, SC_{1-6}alkyl, halo, haloC_{1-6}alkyl, -NH(C=O)OC_{1-6}alkyl, -NH(C=O)OC(C_{1-3}alkyl)$_3$, and wherein C_{1-3}alkyl, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-7}cycloalkyl, aryl and heterocyclyl in each case may be further optionally substituted or R_4 is a chain of 3 or 4 carbon atoms or carbon and heteroatoms which joins with an adjacent B ring atom to form a fused carbocyclylic or heterocycylic ring which is optionally further substituted;

the -C(=O)-W-R_5 moiety is joined to the same Ring B atom as R_4 wherein:

W is O, NH or N(C_{1-6}alkyl);

R_5 is selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, $S(O)_2OH$, $S(O)_2$-C_{1-6}alkyl, or M where M represents a monovalent or divalent cation selected from the group comprising pharmaceutically acceptable cations, such as sodium, potassium, lithium, calcium, magnesium, zinc, ammonium, alkylammonium such as salts formed from triethylamine, alkoxyammonium such as those formed with ethanolamine and salts formed from ethylenediamine, choline or amino acids;

or Z_1 is an alcohol containing group of general formula $(CH_2)_sC(OH)(R_6)(R_7)$ or an ester, carbamate, phosphate, sulfate or prodrug thereof wherein the OH, R_6 and R_7 groups are each attached to the same carbon atom; and

wherein:

s is an integer selected from 0, 1, 2 and 3;

R_6 is H or is selected from optionally substituted C_{1-6}alkyl, optionally substituted C_{2-6}alkenyl, optionally substituted C_{2-6}alkynyl, optionally substituted $(CH_2)_tOC_{1-6}$alkyl, optionally substituted $(CH_2)_tOC(=O)C_{1-6}$alkyl, optionally substituted $(CH_2)_tSC_{1-6}$alkyl, optionally substituted $(CH_2)_tS(=O)C_{1-6}$alkyl, halo, optionally substituted haloC_{1-3}alkyl and optionally substituted $(CH_2)_tNR^aR^b$;

R_7 is selected from optionally substituted C_{1-6}alkyl, optionally substituted C_{2-6}alkenyl, optionally substituted C_{2-6}alkynyl, optionally substituted C_{3-7}cycloalkyl ring, optionally substituted phenyl, optionally substituted 4-6-membered heterocyclyl ring, optionally substituted 5-6-membered heteroaryl ring, optionally substituted $(CH_2)_tOC_{1-6}$alkyl, optionally substituted $(CH_2)_tOC(=O)C_{1-6}$alkyl, optionally substituted $(CH_2)_tSC_{1-6}$alkyl, optionally substituted $(CH_2)_tS(=O)C_{1-6}$alkyl, halo, optionally substituted haloC_{1-3}alkyl and optionally substituted $(CH_2)_tNR^aR^b$;

t is an integer selected from 1, 2, 3, 4, 5 and 6;

or R_6 and R_7 together with the carbon atom to which they are attached form an optionally substituted 4-6-membered heterocyclic ring or C_{3-7}cycloalkyl ring;

and further wherein the prodrug is selected from an ester, carbamate, phosphate or sulfate formed from the hydroxyl moiety;

or Z_1 is a sulfonamide containing group of general formula $(CH_2)_vNRS(=O)_2R_8$ or $(CH_2)_vS(=O)_2NR_9R_{10}$ or a sulfamide containing group of general formula $(CH_2)_vNRS(=O)_2NR_9R_{10}$ wherein:

v is an integer 0, 1, 2 or 3;

R is H or an optionally substituted C_{1-6}alkyl; and

R_8, R_9 and R_{10} are each independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-7}cycloalkyl, phenyl, benzyl, a 3-10-membered heterocyclic ring, a 5-10-membered

heteroaryl ring and further wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-7}cycloalkyl, phenyl, benzyl, a 3-10-membered heterocyclic ring, a 5-10-membered heteroaryl ring may be optionally substituted;

or R_9 and R_{10} may join to form an optionally substituted 3-6-membered heterocyclic ring together with the nitrogen to which they are attached.

2. The use of Claim 1, wherein Z_1 is $(CH_2)_vNRS(=O)_2R_8$, $(CH_2)_vS(=O)_2NR_9R_{10}$ or $(CH_2)_vNRS(=O)_2NR_9R_{10}$.

3. The use according to claim 1 or 2 wherein the polymyxin or polymyxin derivative is selected from an antibacterial polymyxin, an antibacterial polymyxin derivative, a non-antibacterial polymyxin, and a non-antibacterial polymyxin derivative.

4. The use according to any one of claims 1 to 3 wherein the polymyxin is Polymyxin B (PMB) or colistin (Polymyxin E).

5. The use according to any one of claims 1 to 3 wherein the polymyxin derivative is Polymyxin B nonapeptide (PMBN) or a prodrug of colistin.

6. The use according to any one of claims 1 to 5 wherein the polymyxin or polymyxin derivative is provided in a therapeutically effective antibacterial amount or dosage.

7. The use according to any one of claims 1 to 5 wherein the polymyxin or polymyxin derivative is provided in a sub-inhibitory antibacterial MIC amount or dosage.

8. The use according to any one of claims 1 to 7 wherein the combination may be administered concurrently, sequentially or separately to a patient suffering from infection or at risk of infection.

9. The use according to any one of claims 1 to 8 wherein the Gram-negative bacteria or drug resistant Gram-negative bacteria comprises a lipopolysaccharide (LPS) layer.

10. The use according to any one of claims 1 to 8 wherein the Gram-negative bacteria or drug resistant Gram-negative bacteria comprises a lipooligosaccharide (LOS) layer.

11. The use according to any one of claims 1 to 8 wherein the Gram-negative bacteria is one or more bacterial strains selected from the group comprising *E. coli, K. pneumoniae, A. baumannii, P. aeruginosa,* and *Enterobacter spp* and drug resistant strains thereof.

12. The use according to any one of claims 1 to 8 wherein the Gram-negative pathogen is one or more bacterial strains selected from the group comprising *M. catarrhalis, Neisseria, Haemophilus* and *Bordetella* and drug resistant strains thereof.

13. The use according to any one of claims 1 to 8 wherein the Gram-negative pathogen is one or more bacterial strains selected from the group consisting of *L. pneumoniae, C. trachomatis, C. pneumonia, Y. pestis, F. tularensis, B.pseudomallei, C. burnetii, Brucella* species, *B. mallei, C. psittaci* and *R. prowazekii.*

14. The use according to any one of claims 1 to 8 wherein the subject is suffering from or at risk of an intra-abdominal infection (IAI), hospital acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), urinary tract infection (UTI), bacteremias, community acquired bacterial pneumonia (CABP), gonococcal infection (GI), wound or surgical site infections, endocarditis, otitis media, cystic fibrosis or meningitis.

15. Use of a compound of claim 1, in combination with a polymyxin or polymyxin derivative in the preparation of a medicament for the treatment or prevention of a bacterial infection wherein the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and optionally on-target enzyme activity against topoisomerase IV and wherein the bacterial infection is caused by a Gram-negative bacteria or drug resistant Gram-negative bacteria.

16. Use of a compound of claim 1, for improving the antibacterial activity of the compound wherein the use comprises the step of administration of the compound of claim 1 with a polymyxin or polymyxin derivative to a subject suffering from a bacterial infection or at risk of a bacterial infection wherein the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and optionally on-target enzyme activity against topoisomerase IV and wherein the bacterial infection is caused by a Gram-negative bacteria or drug resistant Gram-negative bacteria.

17. The use of a compound of claim 1, or a salt, racemate, diastereomer, enantiomer, ester, carbamate, phosphate, sulfate, deuterated form or prodrug thereof, for improving the antibacterial efficacy of the compound wherein the method comprises the step of administration of the compound with a polymyxin or polymyxin derivative to a subject suffering from a bacterial infection or at risk of a bacterial infection wherein the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and optionally on-target enzyme activity against topoisomerase IV and wherein the bacterial infection is caused by a Gram-negative bacteria or drug resistant Gram-negative bacteria.

18. A composition comprising a compound of claim 1, or a salt, racemate, diastereomer, enantiomer, ester, carbamate, phosphate, sulfate, deuterated form or prodrug thereof, and a polymyxin or polymyxin derivative.

19. An antibacterial agent comprising the compound of claim 1, or a salt, racemate, diastereomer, enantiomer, ester, carbamate, phosphate, sulfate, deuterated form or prodrug thereof, and a polymyxin or polymyxin derivative wherein the bacterial type II topoisomerase inhibitor has on-target enzyme activity against DNA gyrase and optionally on-target enzyme activity against topoisomerase IV.

20. A process for the manufacture of a compound of claim 1, or a salt, racemate, diastereomer, enantiomer, ester, carbamate, phosphate, sulfate, deuterated form or prodrug thereof.

21. A compound of selected from the group consisting of:

A-10) 2-[[5-[2-(Ethylcarbamoylamino)-7-(2-pyridyl)-1,3-benzothiazol-5-yl]pyrimidin-2-yl]sulfamoyl]benzoic acid;

A-11) 1-Ethyl-3-[7-(5-methyl-2-pyridyl)-5-[2-(pyrrolidin-1-ylsulfonylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]urea;

A-12) 1-Ethyl-3-[7-(5-methyl-2-pyridyl)-5-[2-(propylsulfonylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]urea;

A-13) 1-[5-[2-(tert-Butylsulfonylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-14) 1-Ethyl-3-[5-[2-[(2-hydroxy-1,1-dimethyl-ethyl)sulfonylamino]pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-15) 1-Ethyl-3-[5-[2-[[2-hydroxyethyl(methyl)sulfamoyl]amino]pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-16) Methyl 2-[[5-[2-(ethylcarbamoylamino)-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-5-yl]pyrimidin-2-yl]sulfamoyl]acetate;

A-17) 1-[5-[2-(allylsulfonylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-18) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-[2-(dimethylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-19) 1-ethyl-3-[5-[2-(methanesulfonamidomethyl)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-20) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-[4-(2-pyrrolidin-1-ylethyl)piperazin-1-yl]-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-21) 1-[5-[2-(cyclopentylsulfonylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-24) 1-(5-(2-(1,1-dioxido-1,2-thiazinan-2-yl)pyrimidin-5-yl)-7-(pyridin-2-yl)benzo[d]thiazol-2-yl)-3-ethylurea;

A-25) 1-[5-[6-(1,1-dioxo-1,2-thiazolidin-2-yl)-3-pyridyl]-7-(2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethylurea;

A-26) 1-(5-(2-(1,1-dioxidoisothiazolidin-2-yl)pyrimidin-5-yl)-7-(pyridin-2-yl)benzo[d]thiazol-2-yl)-3-ethylurea;

A-27) 1-(5-(2-(1,1-dioxidoisothiazolidin-2-yl)pyrimidin-5-yl)-6-((tetrahydrofuran-2-yl)methoxy)benzo[d]thiazol-2-yl)-3-ethylurea;

A-28) 1-(5-(2-(1,1-dioxidoisothiazolidin-2-yl)pyrimidin-5-yl)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-2-yl)-3-ethylurea;

A-29) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-N-methylmethanesulfonamide;

A-30) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)methanesulfonamide;

A-31) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)methanesulfonamide;

A-32) 1-[5-[2-(dimethylsulfamoylamino)pyrimidin-5-yl]-7-(2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl urea;

A-33) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)propane-1-sulfonamide;

A-34) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)cyclopropanesulfonamide;

A-35) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)cyclopentanesulfonamide;

A-36) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)ethanesulfonamide;

A-37) 1-ethyl-3-[5-[2-(ethylsulfamoylamino)pyrimidin-5-yl]-7-(2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-38) 1-[5-[2-(dimethylsulfamoylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl urea;

A-39) 1-ethyl-3-[5-[2-(ethylsulfamoylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-40) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)cyclopropanesulfonamide;

A-41) 1-ethyl-3-[5-[2-(methylsulfamoylamino)pyrimidin-5-yl]-7-(2-pyridyl)-1,3-benzothiazol-2-yl]urea;

A-42) 1-ethyl-3-[7-(5-methyl-2-pyridyl)-5-[2-(methylsulfamoylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]urea;

A-43) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)morpholine-4-sulfonamide;

A-44) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)morpholine-4-sulfonamide;

A-45) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)pyrrolidine-1-sulfonamide;

A-46) (S)-2-amino-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-phenylpropane-1-sulfonamide;

A-47) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)ethanesulfonamide;

A-48) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)propane-2-sulfonamide;

A-49) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-methoxyazetidine-1-sulfonamide;

A-50) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-methoxyazetidine-1-sulfonamide;

A-51) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)benzenesulfonamide;

A-52) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-morpholinoethanesulfonamide;

A-53) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)pyrrolidine-3-sulfonamide;

A-54) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-hydroxypyrrolidine-1-sulfonamide;

A-55) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-1-(hydroxymethyl)cyclopropane-1-sulfonamide;

A-56) (R)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-morpholinopyrrolidine-1-sulfonamide;

A-57) (R)-3-(dimethylamino)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)pyrrolidine-1-sulfonamide;

A-58) 1-acetyl-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)pyrrolidine-3-sulfonamide;

A-59) (R)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-hydroxypyrrolidine-1-sulfonamide;

A-60) (S)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-3-hydroxypyrrolidine-1-sulfonamide;

A-61) N-(5-(2-(3-ethylureido)-6-fluorobenzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-62) (R)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-(hydroxymethyl)pyrrolidine-1-sulfonamide;

A-63) (S)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)tetrahydrofuran-3-sulfonamide;

A-64) N-(5-(7-bromo-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-65) 1-[7-bromo-5-[6-(tert-butylsulfonylamino)-3-pyridyl]-1,3-benzothiazol-2-yl]-3-ethyl urea;

A-66) methyl 2-[[5-[2-(ethylcarbamoylamino)-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-5-yl]pyrimidin-2-yl]sulfamoyl]acetate;

A-67) (R)-N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-1-(tetrahydro-2H-pyran-2-yl)methanesulfonamide;

A-68) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methoxyethanesulfonamide;

A-69) 1-[5-[6-(tert-butylsulfonylamino)-3-pyridyl]-7-(2-ethylthiazol-4-yl)-1,3-benzothiazol-2-yl]-3-ethyl urea;

A-70) N-(5-(2-(3-ethylureido)-7-(5-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-hydroxyethanesulfonamide;

A-71) N-(5-(2-(3-ethylureido)-7-(1H-pyrazol-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-72) N-(5-(7-(3,5-dimethylisoxazol-4-yl)-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-73) N-(5-(2-(3-ethylureido)-7-(1-methyl-1H-pyrazol-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-74) N-(5-(2-(3-ethylureido)-7-((5-methylpyridin-2-yl)amino)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-75) N-(5-(2-(3-ethylureido)-7-methylbenzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-76) N-(5-(2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-77) N-(5-(7-cyclopropyl-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-78) N-(5-(2-(3-ethylureido)-7-(tetrahydro-2H-pyran-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-79) N-(5-(2-(3-ethylureido)-7-(pyrrolidin-1-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-80) N-(5-(2-(3-ethylureido)-7-(piperazin-1-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-81) N-(5-(2-(3-ethylureido)-7-pyriolinobenzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-82) N-(5-(2-(3-ethylureido)-7-(4-methylpiperazin-1-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-83) N-(5-(7-(4-acetylpiperazin-1-yl)-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-84) N-(5-(2-(3-ethylureido)-7-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-85) N-(5-(2-(3-ethylureido)-7-(4-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-86) N-(5-(2-(3-ethylureido)-7-(5-(morpholinomethyl)pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-87) N-(5-(2-(3-ethylureido)-7-(2-(3-hydroxypyrrolidin-1-yl)thiazol-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-88) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-(2-hydroxy-4-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-89) N-(5-(2-(3-ethylureido)-7-(1-methyl-2-oxo-1,2-dihydropyridin-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-90) 2-(4-(5-(2-(1,1-dimethylethylsulfonamido)pyrimidin-5-yl)-2-(3-ethylureido)benzo[d]thiazol-7-yl)piperazin-1-yl)-N-methylacetamide;

A-91) ethyl 2-(4-(5-(2-(1,1-dimethylethylsulfonamido)pyrimidin-5-yl)-2-(3-ethylureido)benzo[d]thiazol-7-yl)piperazin-1-yl)acetate;

A-92) N-(5-(2-(3-ethylureido)-7-(2-(piperazin-1-yl)thiazol-4-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-93) N-(5-(2-(3-ethylureido)-7-(6-methylpyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-94) N-(5-(7-(2-aminopyridin-3-yl)-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-95) N-(5-(7-(5-aminopyridin-3-yl)-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-96) N-(5-(2-(3-ethylureido)-7-(4-(2-methoxyethyl)piperazin-1-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-97) N-(5-(2-(3-ethylureido)-7-(piperidin-1-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-98) N-(5-(7-(5-(aminomethyl)-2-fluorophenyl)-2-(3-ethylureido)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-99) N-(5-(2-(3-ethylureido)-7-[2-dimethylaminoethyl(methyl)amino]benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-100) N-(5-(2-(3-ethylureido)-7-(pyridin-2-yl)benzo[d]thiazol-5-yl)pyrimidin-2-yl)-2-methylpropane-2-sulfonamide;

A-103) 1-[6-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-5-methoxy-thiazolo[5,4-b]pyridin-2-yl]-3-ethylurea;

A-104) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-(5-hydroxy-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethylurea;

A-105) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-[4-[(cyclopropylamino)methyl]-2-pyridyl]-1,3-benzothiazol-2-yl]-3-ethylurea;

A-106) 1-[7-(5-amino-2-pyridyl)-5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]-3-ethylurea;

A-107) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-(3-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethyl-urea;

A-110) 1-[7-(4-amino-2-pyridyl)-5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]-3-ethylurea;

A-111) 1-[5-[2-(2,3-dihydroxypropylsulfonylamino)pyrimidin-5-yl]-7-(5-methyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethylurea;

A-113) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-(4,5-dimethyl-2-pyridyl)-1,3-benzothiazol-2-yl]-3-ethylurea;

A-114) 1-[5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-7-[(3S,4R,5R,6R)-3,4,5,6-tetrahydroxycyclohexen-1-yl]-1,3-benzothiazol-2-yl]-3-ethylurea; and

A-115) 1-[7-[(3aR,6aR)-2,3,3a,4,6,6a-hexahydro-1H-pyrrolo[2,3-c]pyrrol-5-yl]-5-[2-(tert-butylsulfonylamino)pyrimidin-5-yl]-1,3-benzothiazol-2-yl]-3-ethyl-urea; or

a salt, racemate, diastereomer, enantiomer, ester, carbamate, phosphate, sulfate, deuterated form or prodrug thereof.