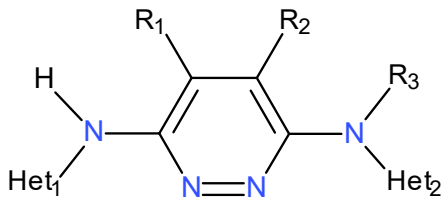
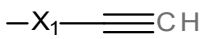
CLAIMS

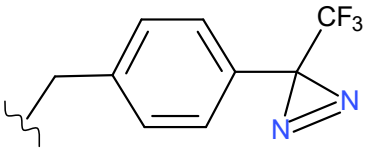
1. Compound of formula (I) :



(I)

wherein:

- R_1 and R_2 independently of one another represent a group selected from: hydrogen; linear or branched C_1-C_6alkyl optionally substituted by a hydroxyl or a C_1-C_6alkoxy group; C_3-C_6cycloalkyl; trifluoromethyl; linear or branched C_1-C_6alkylene-heterocycloalkyl wherein the heterocycloalkyl group is optionally substituted by a a linear or branched C_1-C_6alkyl group;
  or R_1 and R_2 form with the carbon atoms carrying them a C_3-C_6cycloalkylene group,
- R_3 represents a group selected from: hydrogen; C_3-C_6cycloalkyl; linear or branched C_1-C_6alkyl; $-X_1-NR_aR_b$; $-X_1-N^+R_aR_bR_c$; $-X_1-O-R_c$; $-X_1-COOR_c$; $-X_1-PO(OH)_2$; $-X_1-SO_2(OH)$; $-X_1-N_3$ and :
  
  ,
- R_a and R_b independently of one another represent a group selected from: hydrogen; heterocycloalkyl; $-SO_2$-phenyl wherein the phenyl may be substituted by a linear or branched C_1-C_6alkyl; linear or branched C_1-C_6alkyl optionally substituted by one or two hydroxyl groups; C_1-C_6alkylene-SO_2OH; C_1-C_6alkylene-SO_2O^-; C_1-C_6alkylene-COOH; C_1-C_6alkylene-$PO(OH)_2$; C_1-C_6alkylene-NR_dR_e; C_1-C_6alkylene-$N^+R_dR_eR_f$; C_1-C_6alkylene-phenyl wherein the phenyl may be substituted by a C_1-C_6alkoxy group;
  the group:



or R_a and R_b form with the nitrogen atom carrying them a

cycle B_1;

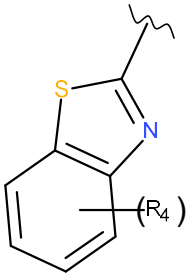
or R_a, R_b and R_c form with the nitrogen atom carrying them a bridged C_3-C_8heterocycloalkyl,

- R_c, R_d, R_e, R_f, independently of one another represents a hydrogen or a linear or branched C_1-C_6alkyl group,

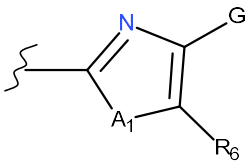
  or R_d and R_e form with the nitrogen atom carrying them a a cycle B_2,

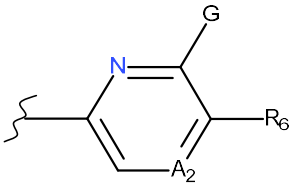
  or R_d, R_e and R_f form with the nitrogen atom carrying them a bridged C_3-C_8heterocycloalkyl,

- Het_1 represents the following group:



- Het_2 represents a group selected from:





- A_1 is –NH-, -N(C_1-C_3alkyl), O, S or Se,
- A_2 is N, CH or C(R_5),
- G is selected from the group consisting of:

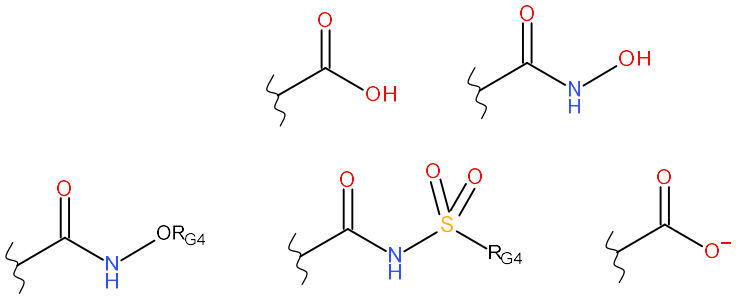
-C(O)OR_{G3}, -C(O)N$R_{G1}R_{G2}$, -C(O)R_{G2}, -NR_{G1}C(O)R_{G2},

- R_{G1} and R_{G2} at each occurrence are each independently selected from the group consisting of hydrogen, C_1-C_6alkyl optionally substituted by 1 to 3 halogen atoms, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_6cycloalkyl, phenyl and -$(CH_2)_{1-4}$-phenyl;

- R_{G3} is selected from the group consisting of C_1-C_6alkyl optionally substituted by 1 to 3 halogen atoms, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_6cycloalkyl, phenyl and -$(CH_2)_{1-4}$-phenyl; or

R_{G1} and R_{G2}, together with the atom to which each is attached are combined to form a C_3-

C_8heterocycloalkyl ; or in the alternative, G is selected from the group consisting of:



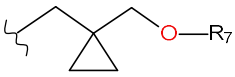
wherein R_{G4} is selected from C_1-C_6alkyl optionally substituted by 1 to 3 halogen atoms, C_2-C_6alkenyl, C_2-C_6alkynyl and C_3-C_6cycloalkyl,

- R_4 represents a hydrogen, fluorine, chlorine or bromine atom, a methyl, a hydroxyl or a methoxy group,
- R_5 represents a group selected from: C_1-C_6alkyl optionally substituted by 1 to 3 halogen atoms; C_2-C_6alkenyl; C_2-C_6alkynyl; halogen or –CN,
- R_6 represents a group selected from:

hydrogen;

-C_2-C_6alkenyl;

-X_2-O-R_7;



;

-X_2-NSO_2-R_7;

-C=C(R_9)-Y_1-O-R_7;

C_3-C_6cycloalkyl;

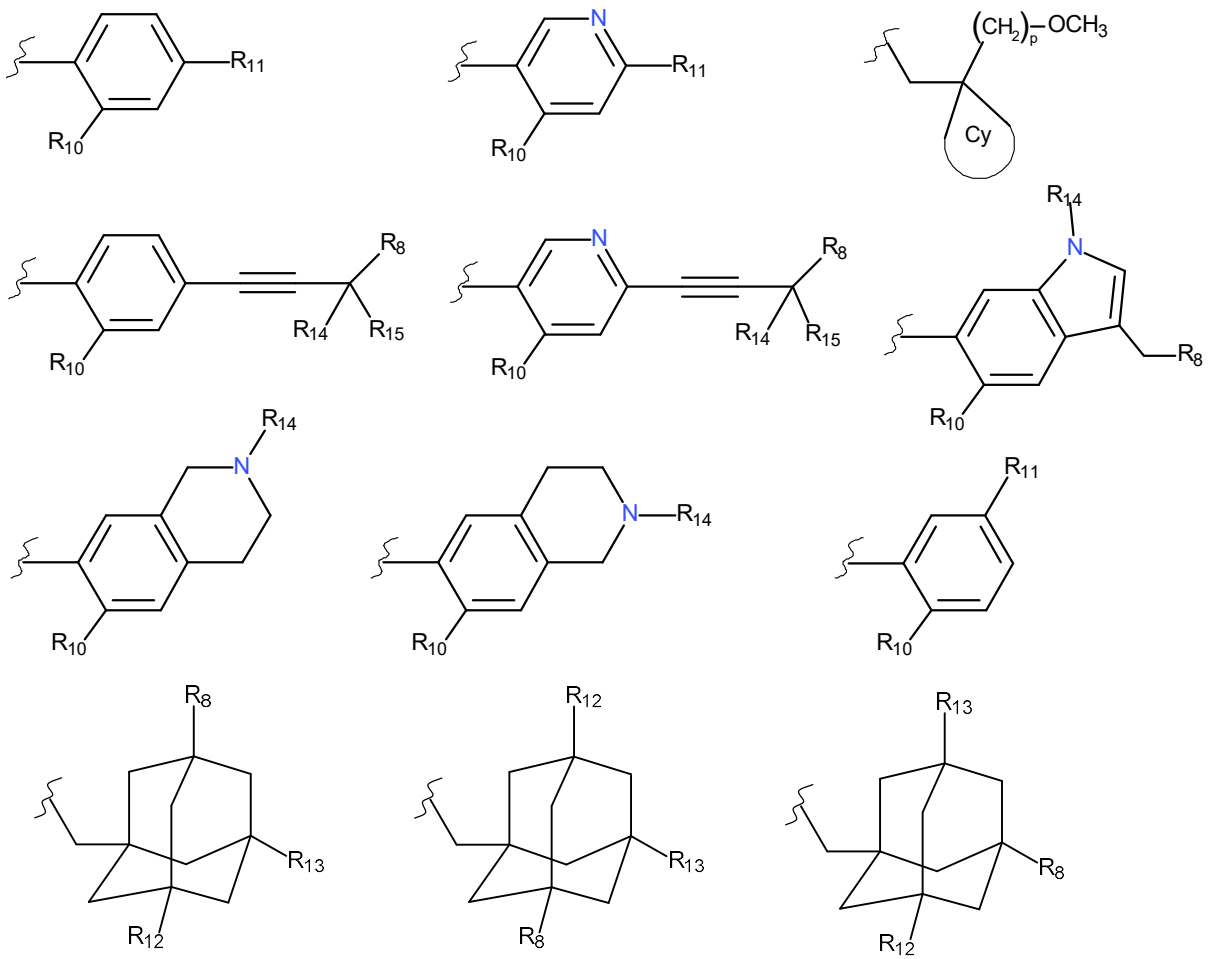
C_3-C_6heterocycloalkyl optionally substituted by a hydroxyl group;

C_3-C_6cycloalkylene-Y_2-R_7 ;

C_3-C_6heterocycloalkylene-Y_2-R_7 group,

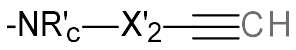
an heteroarylene-R_7 group optionally substituted by a linear or branched C_1-C_6alkyl group,

- R_7 represents a group selected from: linear or branched C_1-C_6alkyl group; (C_3-C_6)cycloalkylene-R_8; or:



wherein Cy represents a C_3-C_8cycloalkyl,

- R_8 represents a group selected from: hydrogen; linear or branched C_1-C_6alkyl, -NR'$_a$R'$_b$; -NR'$_a$-CO-OR'$_c$; -NR'$_a$-CO-R'$_c$; -N$^+$R'$_a$R'$_b$R'$_c$; -O-R'$_c$; -NH-X'$_2$-N$^+$R'$_a$R'$_b$R'$_c$; -O-X'$_2$-NR'$_a$R'$_b$, -X'$_2$-NR'$_a$R'$_b$, -NR'$_c$-X'$_2$-N$_3$ and :

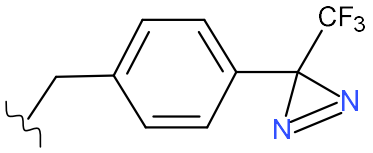


,

- R_9 represents a group selected from linear or branched C_1-C_6alkyl, trifluoromethyl, hydroxyl, halogen, C_1-C_6alkoxy,
- R_{10} represents a group selected from hydrogen, fluorine, chlorine, bromine, -CF_3 and methyl,
- R_{11} represents a group selected from hydrogen, C_1-C_3alkylene-R_8, -O-C_1-C_3alkylene-R_8, -CO-NR_hR_i and -CH=CH-C_1-C_4alkylene-NR_hR_i, -CH=CH-CHO, C_3-C_8cycloalkylene-CH_2-R_8, C_3-C_8heterocycloalkylene-CH_2-R_8,

- R_{12} and R_{13}, independently of one another, represent a hydrogen atom or a methyl group,
- R_{14} and R_{15}, independently of one another, represent a hydrogen or a methyl group, or R_{14} and R_{15} form with the carbon atom carrying them a a cyclohexyl,
- R_h and R_i, independently of one another, represent a hydrogen or a linear or branched C_1-C_6alkyl group,
- X_1 and X_2 independently of one another, represent a linear or branched C_1-C_6alkylene group optionally substituted by one or two groups selected from trifluoromethyl, hydroxyl, halogen, C_1-C_6alkoxy,
- X'_2 represents a linear or branched C_1-C_6alkylene,
- R'_a and R'_b independently of one another, represent a group selected from: hydrogen; heterocycloalkyl; -SO_2-phenyl wherein the phenyl may be substituted by a linear or branched C_1-C_6alkyl; linear or branched C_1-C_6alkyl optionally substituted by one or two hydroxyl or C_1-C_6alkoxy groups; C_1-C_6alkylene-SO_2OH; C_1-C_6alkylene-SO_2O^-; C_1-C_6alkylene-COOH; C_1-C_6alkylene-$PO(OH)_2$; C_1-C_6alkylene-$NR'_dR'_e$; C_1-C_6alkylene-$N^+R'_dR'_eR'_f$; C_1-C_6alkylene-O-C_1-C_6alkylene-OH; C_1-C_6alkylene-phenyl wherein the phenyl may be substituted by a hydroxyl or a C_1-C_6alkoxy group;

  the group:



  or R'_a and R'_b form with the nitrogen atom carrying them a cycle B_3,

  or R'_a, R'_b and R'_c form with the nitrogen atom carrying them a bridged C_3-C_8heterocycloalkyl,

- R'_c, R'_d, R'_e, R'_f, independently of one another, represents a hydrogen or a linear or branched C_1-C_6alkyl group,

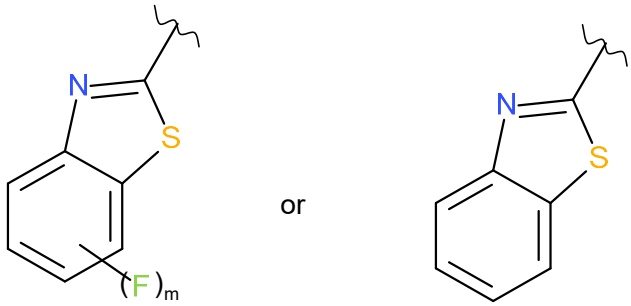
  or R'_d and R'_e form with the nitrogen atom carrying them a cycle B_4,

  or R'_d, R'_e and R'_f form with the nitrogen atom carrying them a bridged C_3-C_8heterocycloalkyl,

- Y_1 represents a linear or branched C_1-C_4alkylene,
- Y_2 represents a bond, -O-, -O-CH_2-, -O-CO-, -O-SO_2-, -CH_2-, -CH_2-O, -CH_2-CO-, -CH_2-SO_2-,-C_2H_5-, -CO-, -CO-O-, -CO-CH_2-, -CO-NH-CH_2-, -SO_2-, -SO_2-CH_2-, -NH-CO-, -NH-SO_2-,
- m=0, 1 or 2,
- p=1, 2, 3 or 4,
- B_1, B_2, B_3 and B_4, independently of one another, represents a C_3-C_8heterocycloalkyl group, which group can: (i) be a mono- or bi-cyclic group, wherein bicyclic group includes fused, briged or spiro ring system, (ii) can contain, in addition to the nitrogen atom, one or two hetero atoms selected independently from oxygen, sulphur and nitrogen, (iii) be substituted by one or two groups selected from: fluorine, bromine, chlorine, linear or branched C_1-C_6alkyl, hydroxyl, –NH_2, oxo or piperidinyl,

its enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

2. Compound according to claim 1 wherein Het_1 represents:



3. Compound according to claim 1 or 2 wherein R_1 represents a methyl group and R_2 represents a hydrogen atom.

4. Compound according to claim 1 or 2 wherein R_1 and R_2 represent each a methyl group or a hydrogen atom.

5. Compound according to claim 1 or 2 wherein R_1 or R_2 represents a linear or branched C_1-C_6alkyl optionally substituted by a hydroxyl or a C_1-C_6alkoxy group, preferably a group selected from: methyl, methoxymethyl, hydroxymethyl, ethyl and prop-2-yl.

6. Compound according to claim 1 or 2 wherein R_1 or R_2 represents a C_3-C_6cycloalkyl, preferably a cyclopropyl group.

7. Compound according to claim 1 or 2 wherein R_1 represents a trifluoromethyl group.

8. Compound according to claim 1 or 2 wherein R_2 represents a linear or branched C_1-C_6alkylene-heterocycloalkyl, preferably a (4-methyl-piperazin-1-yl)propyl group.

9. Compound according to claim 1 or 2 wherein R_1 and R_2 form with the carbon atoms carrying them a cyclohexene or a cyclopentene group.

10. Compound according to any of claims 1 to 9 wherein R_3 represents a hydrogen atom or a methyl group.

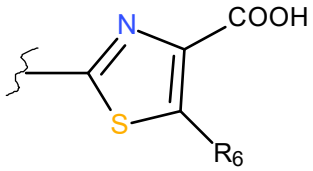
11. Compound according to any of claims 1 to 9 wherein R_3 represents $-X_1-PO(OH)_2$, $-X_1-SO_2(OH)$, $-X_1-NR_aR_b$; $-X_1-N^+R_aR_bR_c$, wherein R_a or R_b, or both of them, represent a group selected from C_1-C_6alkylene-SO_2OH, C_1-C_6alkylene-SO_2O^- and C_1-C_6alkylene-$PO(OH)_2$.

12. Compound according to any of claims 1 to 9 wherein R_8 represents $-NR'_aR'_b$; $-N^+R'_aR'_bR'_c$; $-NH-X'_2-N^+R'_aR'_bR'_c$, wherein R'_a and R'_b, or both of them, represent a group selected from C_1-C_6alkylene-SO_2OH and C_1-C_6alkylene-$PO(OH)_2$.

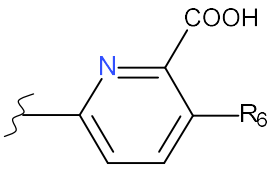
13. Compound according to any of claims 1 to 9 wherein R_3 represents a group selected from: ethyl, propyl; 2-methoxy-ethyl, 2-(morpholin-4-yl)ethyl, 3-(morpholin-4-yl)propyl, 3-diethylamino-propyl, 3-methoxy-propyl, 3-hydroxy-propyl, 3,4-dihydroxy-butyl, 4-methoxy-3-hydroxy-butyl, 4-hydroxy-3-methoxy-butyl, 2,3-dihydroxy-propyl, 4,5-dihydroxy-pentyl, 4-hydroxy-butyl, 3-hydroxy-2-morpholino-propyl, 5-hydroxy-4-methoxy-pentyl, 5-morpholino-4-hydroxy-pentyl, 3-hydroxy-2-methoxy-propyl, 5-[2-(dimethylamino)ethyl-methyl-amino]-4-hydroxy-pentyl, 5-hydroxy-pentyl, 5-methoxy-4-hydroxy-pentyl, 5-(dimethylamino)-4-hydroxy-pentyl, 4-hydroxy-5-(trimethylammonio)pentyl, 5-[3-sulfonate-propyl-dimethyl-ammonio]-4-hydroxy-pentyl, 4-hydroxy-5-(methylamino)pentyl, 3-carboxy-propyl, 5-[methyl(4-piperidyl)amino]pentyl, 5-(2-morpholinoethylamino)pentyl, 5-[2-(4-methyl-piperazin-1-yl)ethylamino)pentyl, 4-[2-(4-methyl-piperazin-1-yl)ethylamino)butyl, 4-hydroxy-5-[methyl-[2-(methylamino)ethyl]amino]pentyl, 5-[2-

(diethylamino)ethylamino]-4-hydroxy-pentyl, 5-(4-Amino-1-piperidyl)-4-hydroxy-pentyl, 4-hydroxy-5-piperazin-1-yl-pentyl, 5-[2-(1-piperidyl)ethylamino]pentyl, 4-(4-Amino-1-piperidyl)butyl, 4-[2-(diethylamino)ethylamino]butyl, 5-(4-Amino-1-piperidyl)pentyl, 4-[methyl-[2-(methylamino)ethyl]amino]butyl, 4-(2-morpholinoethylamino)butyl, 4-[2-(4-methyl-piperazin-1-yl)ethylamino)butyl, 4-[(1-methyl-4-piperidyl)amino]butyl, 5-[2-(diethylamino)ethylamino]pentyl, 4-piperazin-1-ylbutyl, 4-(methylamino)butyl, 5-piperazin-1-ylpentyl, 5-[methyl-[2-(methylamino)ethyl, 5-aminopentyl, 4-aminobutyl, 5-(methylamino)pentyl, 5-[3-(4-methylpiperazin-1-yl)propylamino]pentyl, 4-hydroxy-5-[methyl(2-phosphonoethyl)amino]pentyl, 6-(dimethylamino)hexyl, 3-(dimethylamino)propyl, 2-(trimethylammonio)ethyl, 3-(trimethylammonio)propyl, 2-(dimethylamino)ethyl, 4-(dimethylamino)butyl, 5-[3-sulfonate-propyl-dimethyl-ammonio]pentyl, 4-(trimethylammonio)butyl, 4-hydroxy-5-quinuclidin-1-ium-1-yl-pentyl, 4-hydroxy-5-(1-aza-4-azoniabicyclo[2.2.2]octan-4-yl)pentyl, 4-hydroxy-5-(4-methylmorpholin-4-ium-4-yl)pentyl, 5-(trimethylammonio)pentyl, 4-hydroxy-5-(1-methylpiperidin-1-ium-1-yl)pentyl, 5-(1,4-dimethylpiperazin-1-ium-1-yl)-4-hydroxy-pentyl, 6-(trimethylammonio)hexyl, 5-[3-hydroxypropyl(dimethyl)ammonio]pentyl, 5-[2-hydroxyethyl(dimethyl)ammonio]pentyl, 5-[carboxymethyl(dimethyl)ammonio]pentyl, 5-[carboxymethyl(dimethyl)ammonio]pentyl, 3-phosphonopropyl, 3-[3-sulfonate-propyl-dimethyl-ammonio]propyl, 3-sulfopropyl, 4-sulfobutyl, 4-phosphonobutyl, 4-carboxybutyl, 3-aminopropyl, 3-azidopropyl, pent-4-yn-1-yl, 4-aminobutyl, 4-azidobutyl, hex-5-yn-1-yl, 5-azidopentyl.

14. Compound according to any of claims 1 to 13 wherein Het_2 represents:



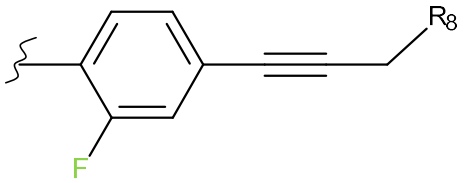
15. Compound according to any of claims 1 to 13 wherein Het_2 represents:



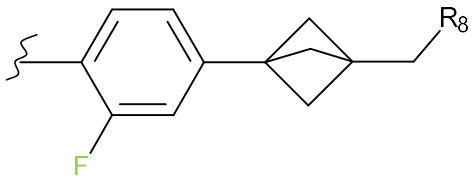
16. Compound according to claim 14 or 15 wherein R_6 represents a hydrogen atom.

17. Compound according to claim 14 wherein R_6 represents a $–X_2-O-R_7$ group wherein X_2 is a propylene group.

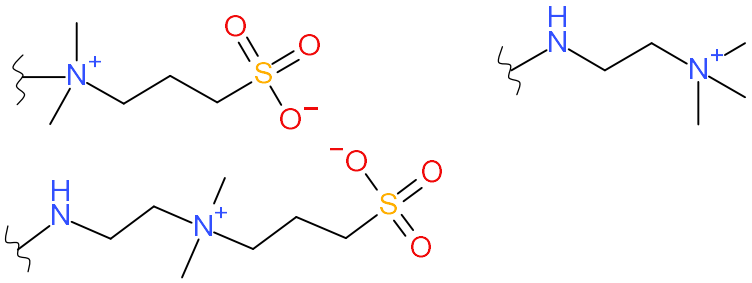
18. Compound according to claim 17 wherein R_7 represents the following group:



19. Compound according to claim 17 wherein R_7 represents the following group:

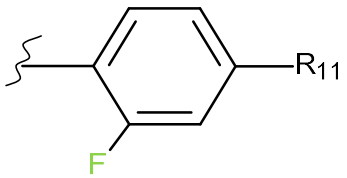


20. Compound according to claim 18 or 19 wherein R_8 represents a group selected from: dimethylamino, methylamino, methylethylamino, diethylamino, methyl[2-(methylamino)ethyl]amino, (2-hydroxyethyl)(methyl)amino, 4-morpholinyl, pyrrolidin-1-yl, 1-piperidyl, [(*tert*-butoxy)carbonyl](methyl)amino, hydroxyl, bis(3-sulfopropyl)amino, 3-sulfopropylamino, methyl(3-sulfopropyl)amino, methyl(p-tolylsulfonyl)amino, (4-methoxyphenyl)methyl-methyl-amino, 2-(dimethylamino)ethylamino and :



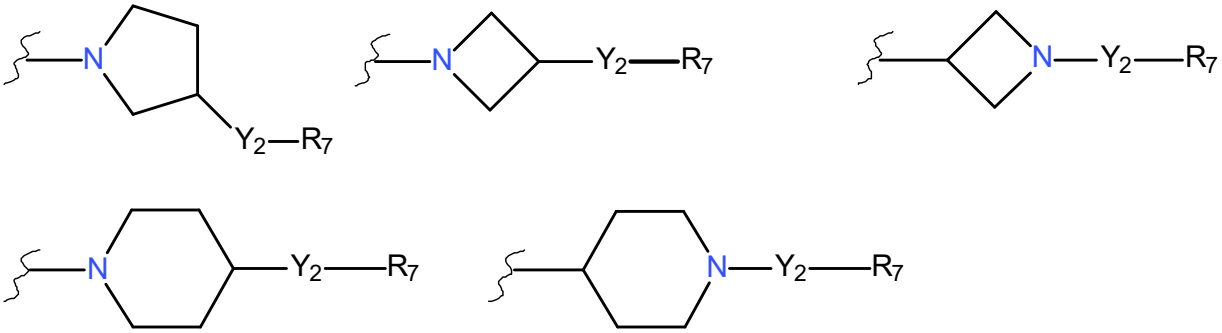
21. Compound according to claim 18 or 19 wherein R_8 represents a group selected from: 3-piperazin-1-yl, 4-methylpiperazin-1-yl, 3-hydroxypropyl(methyl)amino, [(3*S*)-3,4-dihydroxybutyl]-methyl-amino, 3-hydroxypropylamino, [(3*S*)-3,4-dihydroxybutyl]amino, 4-hydroxybutyl(methyl)amino, [(3*R*)-3,4-dihydroxybutyl]-methyl-amino, 4-hydroxybutylamino, [(3*R*)-3,4-dihydroxybutyl]amino.

22. Compound according to claim 17 wherein R_7 represents:



wherein R_{11} is selected from dimethylcarbamoyl, 3-(dimethylamino)propyl, 3-(methylamino)propyl.

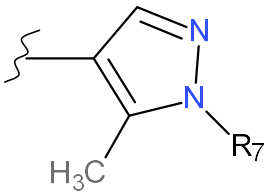
23. Compound according to claim 14 wherein R_6 represents a C_3-C_6heterocycloalkylene-Y_2-R_7 group wherein the heterocycloalkylene group is selected from:



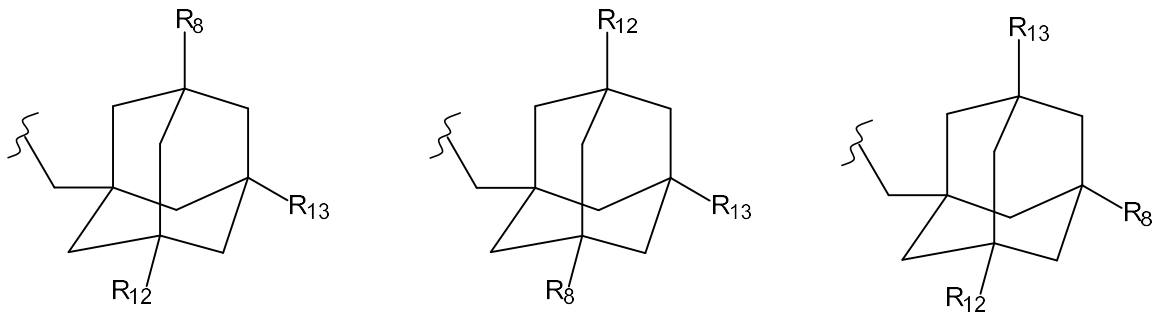
24. Compound according to claim 23 wherein R_7 is selected from: methyl, methylethyl, *tert*-butyl, 2-methylpropyl and phenyl, preferably phenyl.

25. Compound according to claim 14 or 15 wherein R_6 represents -C=C(R_9)-Y_1-O-R_7 wherein Y_1 is a methylene group.

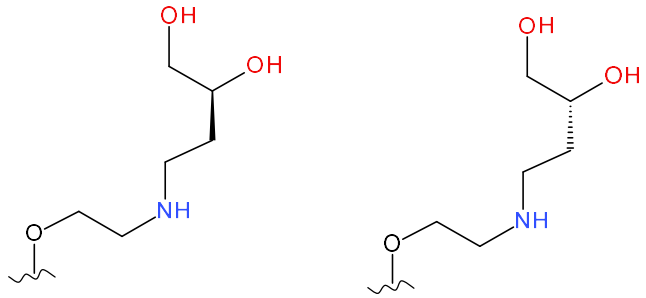
26. Compound according to claim 14 or 15 wherein R_6 represents:



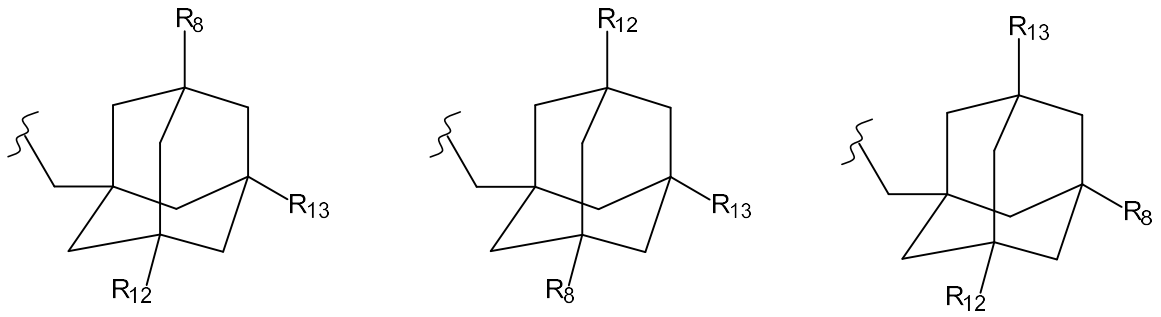
27. Compound according to claim 26 wherein R_7 represents a group selected from :



wherein R_8 represents a group selected from: hydrogen, 2-(methylamino)ethoxy and:



28. The compound according to claim 26 wherein R_7 represents a group selected from :



wherein R_8 represents a group selected from: 2-(dimethylamino)ethoxy, 2-[(2-sulfoethyl)amino]ethoxy, 2-[methyl(2-sulfoethyl)amino]ethoxy, 2-(3-hydroxypropylamino)ethoxy, 2-(3-methoxypropylamino)ethoxy, 2-morpholinoethoxy, 2-(2-carboxyethylamino)ethoxy, 2-[(3-hydroxyphenyl)methylamino]ethoxy, 2-(methylamino)ethoxy, 2-pyrrolidin-1-ylethoxy, 2-(4-methylpiperazin-1-yl)ethoxy, 2-(4-hydroxybutylamino)ethoxy, 2-piperazin-1-ylethoxy, 2-[3-hydroxypropyl(methyl)amino]ethoxy, 2-[4-hydroxybutyl(methyl)amino]ethoxy; 2-[[3-hydroxy-2-(hydroxymethyl)propyl]amino]ethoxy; 2-[bis(3-hydroxypropyl)amino]ethoxy.

29. A compound according to claim 1 selected in the following group:

- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(4-hydroxybutyl)amino)-5-(3-{2-fluoro-4-[3-(methylamino)prop-1-yn-1-yl]phenoxy}propyl)-1,3-thiazole-4-carboxylic

acid,

- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(methyl)amino)-5-(3-{2-fluoro-4-[3-(methylamino)prop-1-yn-1-yl]phenoxy}propyl)-1,3-thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-(3,4-dihydroxybutyl)amino]-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-(3-hydroxy-4-methoxy-butyl)amino]-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-(2,3-dihydroxypropyl)amino]-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-(4,5-dihydroxypentyl)amino]-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-(3,4-dihydroxybutyl)amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-(3-hydroxypropyl)amino]-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-[4-hydroxy-5-(trimethylammonio)pentyl]amino]-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylate,
- 3-[[5-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-[4-carboxy-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]thiazol-2-yl]amino]-2-hydroxy-pentyl]-dimethyl-ammonio]propane-1-sulfonate,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-(4-hydroxybutyl)amino]-5-[3-[2-fluoro-4-[3-[methyl(3-sulfopropyl)amino]prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylic acid,
- 5-{1-[(Adamantan-1-yl)methyl]-5-methyl-1*H*-pyrazol-4-yl}-2-({6-[(1,3-benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(methyl)amino)-1,3-thiazole-4-carboxylic acid,
- 5-{1-[(Adamantan-1-yl)methyl]-5-methyl-1*H*-pyrazol-4-yl}-2-({6-[(1,3-benzothiazol-2-yl)amino]-5-cyclopropylpyridazin-3-yl}(methyl)amino)-1,3-thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-[5-[2-(diethylamino)ethylamino]-4-hydroxy-pentyl]amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylic acid,

- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-[5-[2-(4-methylpiperazin-1-yl)ethylamino]pentyl]amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-(4-hydroxy-5-piperazin-1-yl-pentyl)amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(methyl)amino)-5-[(2*S*)-3-{4-[3-(dimethylamino)prop-1-yn-1-yl]-2-fluorophenoxy}-2-methylpropyl]-1,3-thiazole-4-carboxylic acid,
- 2-[4-Aminobutyl-[6-(1,3-benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[5-Aminopentyl-[6-(1,3-benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-[3-(dimethylamino)propyl]amino]-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-5-[3-[4-[3-(dimethylamino)but-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-[4-hydroxy-5-(trimethylammonio)pentyl]amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylate,
- 3-[2-[3-[4-[3-[2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-4-carboxy-thiazol-5-yl]propoxy]-3-fluoro-phenyl]prop-2-ynylamino]ethyl-dimethyl-ammonio]propane-1-sulfonate,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-[4-hydroxy-5-(4-methylmorpholin-4-ium-4-yl)pentyl]amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylate,
- 2-[3-[4-[3-[2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-4-carboxy-thiazol-5-yl]propoxy]-3-fluoro-phenyl]prop-2-ynylamino]ethyl-trimethyl-ammonium,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-[6-(trimethylammonio)hexyl]amino]-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylate,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-[5-[2-

hydroxyethyl(dimethyl)ammonio]pentyl]amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylate,

- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-[5-[carboxymethyl(dimethyl)ammonio]pentyl]amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylate,
- 3-[[5-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-[4-carboxy-5-[3-[2-fluoro-4-[(*E*)-3-oxoprop-1-enyl]phenoxy]propyl]thiazol-2-yl]amino]-2-hydroxy-pentyl]-dimethyl-ammonio]propane-1-sulfonate,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-5-[3-[4-[1-[(dimethylamino)methyl]-3-bicyclo[*1.1.1*]pentanyl]phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-Benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-(3-phosphonopropyl)amino]-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(3-carboxypropyl)amino)-5-(3-{4-[3-(dimethylamino)prop-1-yn-1-yl]-2-fluorophenoxy}propyl)-1,3-thiazole-4-carboxylic acid,
- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(3-phosphonopropyl)amino)-5-(3-{4-[3-(dimethylamino)prop-1-yn-1-yl]-2-fluorophenoxy}propyl)-1,3-thiazole-4-carboxylic acid,
- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(3-sulfopropyl)amino)-5-(3-{4-[3-(dimethylamino)prop-1-yn-1-yl]-2-fluorophenoxy}propyl)-1,3-thiazole-4-carboxylic acid,
- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(4-sulfobutyl)amino)-5-(3-{4-[3-(dimethylamino)prop-1-yn-1-yl]-2-fluorophenoxy}propyl)-1,3-thiazole-4-carboxylic acid,
- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(4-phosphonobutyl)amino)-5-(3-{4-[3-(dimethylamino)prop-1-yn-1-yl]-2-fluorophenoxy}propyl)-1,3-thiazole-4-carboxylic acid,
- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(4-carboxybutyl)amino)-5-(3-{4-[3-(dimethylamino)prop-1-yn-1-yl]-2-fluorophenoxy}propyl)-1,3-thiazole-4-carboxylic acid,
- 2-[{6-[(1,3-benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(pent-4-yn-1-yl)amino]-5-(3-{2-fluoro-4-[3-(methylamino)prop-1-yn-1-yl]phenoxy}propyl)-1,3-thiazole-4-carboxylic

acid,

- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(methyl)amino)-5-{3-[2-fluoro-4-(3-{methyl[2-(methylamino)ethyl]amino}prop-1-yn-1-yl)phenoxy]propyl}-1,3-thiazole-4-carboxylic acid,
- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(methyl)amino)-5-[3-(2-fluoro-4-{3-[(2-hydroxyethyl)(methyl)amino]prop-1-yn-1-yl}phenoxy)propyl]-1,3-thiazole-4-carboxylic acid,
- 2-({6-[(1,3-Benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(methyl)amino)-5-{3-[2-fluoro-4-(3-hydroxyprop-1-yn-1-yl)phenoxy]propyl}-1,3-thiazole-4-carboxylic acid,
- 2-[5-azidopentyl-[6-[(1,3-benzothiazol-2-yl)amino]-5-methyl-pyridazin-3-yl]amino]-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]-1,3-thiazole-4-carboxylic acid,

its enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

30. A compound according to claim 1 selected in the following group:

- 6-[{6-[(1,3-benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(methyl)amino]-3-[1-({3-[2-(dimethylamino)ethoxy]-5,7-dimethyladamantan-1-yl}methyl)-5-methyl-1*H*-pyrazol-4-yl]pyridine-2-carboxylic acid,
- 6-[[6-(1,3-benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-3-[1-[[3-[2-(3-hydroxypropylamino)ethoxy]-5,7-dimethyl-1-adamantyl]methyl]-5-methyl-pyrazol-4-yl]pyridine-2-carboxylic acid,
- 6-[[6-(1,3-benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-3-[1-[[3-[2-(3-methoxypropylamino)ethoxy]-5,7-dimethyl-1-adamantyl]methyl]-5-methyl-pyrazol-4-yl]pyridine-2-carboxylic acid,
- 6-[{6-[(1,3-benzothiazol-2-yl)amino]-5-methylpyridazin-3-yl}(methyl)amino]-3-(1-{[3-(2-{[(3*S*)-3,4-dihydroxybutyl]amino}ethoxy)-5,7-dimethyladamantan-1-yl]methyl}-5-methyl-1*H*-pyrazol-4-yl)pyridine-2-carboxylic acid,
- 6-[[6-(1,3-benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-3-[1-[[3,5-dimethyl-7-(2-morpholinoethoxy)-1-adamantyl]methyl]-5-methyl-pyrazol-4-yl]pyridine-2-carboxylic acid,
- 6-[[6-(1,3-benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-3-[1-[[3-[2-(2-carboxyethylamino)ethoxy]-5,7-dimethyl-1-adamantyl]methyl]-5-methyl-pyrazol-4-yl]pyridine-2-carboxylic acid,
- 6-[[6-(1,3-benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-3-[1-[[3-[2-[(3-

hydroxyphenyl)methylamino]ethoxy]-5,7-dimethyl-1-adamantyl]methyl]-5-methyl-pyrazol-4-yl]pyridine-2-carboxylic acid,

- 2-[[6-(1,3-benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-5-[3-[4-[3-(dimethylamino)prop-1-ynyl]-2-fluoro-phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-(3-hydroxypropyl)amino]-5-[3-[2-fluoro-4-[3-(methylamino)prop-1-ynyl]phenoxy]propyl]thiazole-4-carboxylic acid,
- 2-[[6-(1,3-benzothiazol-2-ylamino)-5-methyl-pyridazin-3-yl]-methyl-amino]-5-[3-[2-fluoro-4-(3-pyrrolidin-1-ylprop-1-ynyl)phenoxy]propyl]thiazole-4-carboxylic acid,

its enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

31. Pharmaceutical composition comprising a compound according to any of claims 1 to 30, or an addition salt thereof with a pharmaceutically acceptable acid or base in combination with one or more pharmaceutically acceptable excipients.

32. Pharmaceutical composition according to claim 31 for use as pro-apoptotic agents.

33. Pharmaceutical composition according to claim 31 for use in the treatment of cancers, auto-immune diseases or immune system diseases.

34. Pharmaceutical composition for use according to claim 33 wherein the cancer is an haematological malignancy or a solid tumor.

35. Pharmaceutical composition for use according to claim 34 wherein the haematological malignancy is myeloma, especially multiple myeloma, lymphoma, especially Non-Hodgkin Lymphoma (NHL), or leukemia, especially Chronic Lymphocytic Leukemia (CLL), T-cell Acute Lymphoblastic Leukemia (T-ALL), B-cell Acute Lymphoblastic Leukemia (B-ALL) and Acute Myelogenous Leukemia (AML).

36. Pharmaceutical composition for use according to claim 34 wherein the solid tumor is selected from bladder, brain, breast, uterus, œsophagus and liver cancers, colorectal cancer, renal cancer, melanoma, ovarian cancer, prostate cancer, pancreatic cancer and lung cancer.

37. Compound according to any of claims 1 to 30, or an addition salt thereof with a pharmaceutically acceptable acid or base, for use in the treatment of a cancer selected from: myeloma, especially multiple myeloma, lymphoma, especially Non-Hodgkin Lymphoma (NHL), or leukemia, especially Chronic Lymphocytic Leukemia (CLL), T-cell Acute Lymphoblastic Leukemia (T-ALL), B-cell Acute Lymphoblastic Leukemia (B-ALL) and Acute Myelogenous Leukemia (AML), bladder, brain, breast, uterus, œsophagus and liver cancers, colorectal cancer, renal cancer, melanoma, ovarian cancer, prostate cancer, pancreatic cancer and lung cancer, especially non-small-cell lung cancer and small-cell lung cancer.

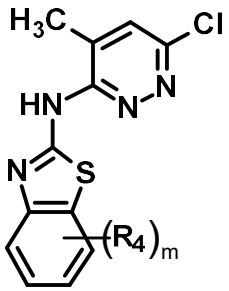
38. Combination of a compound according to any of claims 1 to 30, with an anti-cancer agent selected from genotoxic agents, mitotic poisons, anti-metabolites, proteasome inhibitors, kinase inhibitors and antibodies.

39. Pharmaceutical composition comprising a combination according to claim 38 in combination with one or more pharmaceutically acceptable excipients.

40. Combination according to claim 38 for use in the treatment of cancers.

41. Compound according to any of claims 1 to 30, for use in the treatment of cancers requiring radiotherapy.

42. Synthesis intermediate which is:



wherein R_4 and m are as defined in general formula (I), preferably R_4 represents a hydrogen atom.