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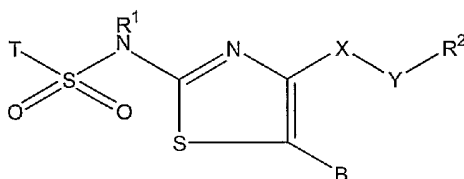
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(54) Title: NEW USE I



(I)

(57) **Abstract:** The invention relates to a method for pro-
moting wound healing, said method comprising adminis-
tering to a mammal, including man, in need of such promo-
tion an effective amount of an inhibitor of 11-b-hydroxys-
teroid dehydrogenase type 1, wherein the said 11b-HSD1
inhibitor has the formula (I) wherein T, B, X, Y, R1 and
R2 are as defined in the specification. These compounds
may also be used in the manufacture of a medicament for
promoting wound healing.



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NEW USE I

RELATED APPLICATIONS

This application claims priority to Swedish application number 0301882-7, filed on June 25, 2003, the contents of which are incorporated herein by reference.

TECHNICAL FIELD

The present invention relates to the use of chemical compounds for wound healing, said
5 compounds acting on the human 11- β -hydroxysteroid dehydrogenase type 1 enzyme (11 β HSD1).

BACKGROUND ART

10 Cortisol performs a broad range of metabolic functions and other functions. The multitude of glucocorticoid action is exemplified in patients with prolonged increase in plasma glucocorticoids, so called "Cushing's syndrome". Patients with Cushing's syndrome have prolonged increase in plasma glucocorticoids and exhibit impaired glucose tolerance, type 2 diabetes, central obesity, and osteoporosis. These patients also
15 have impaired wound healing and brittle skin (1).

Glucocorticoids have been shown to increase risk of infection and delay healing of open wounds (2). Patients treated with glucocorticoids have 2-5-fold increased risk of complications when undergoing surgery (3).

20

The European patent application No. EP 0902288 discloses a method for diagnosing the status of wound healing in a patient, comprising detecting cortisol levels in said wound. The authors suggest that elevated levels of cortisol in wound fluid, relative to normal plasma levels in healthy individuals, correlates with large, non-healing wounds (4).

25

In humans, the 11 β -HSD catalyzes the conversion of cortisol to cortisone, and vice versa. The parallel function of 11 β -HSD in rodents is the interconversion of

corticosterone and 11-dehydrocorticosterone (5). Two isoenzymes of 11 β -HSD, 11 β -HSD1 and 11 β -HSD2, have been characterized, and differ from each other in function and tissue distribution (6). Like GR, 11 β -HSD1 is expressed in numerous tissues like liver, adipose tissue, adrenal cortex, gonads, lung, pituitary, brain, eye etc (7-9). The
5 function of 11 β -HSD1 is to fine-tune local glucocorticoid action. 11 β -HSD activity has been shown in the skin of humans and rodents, in human fibroblasts and in rat skin pouch tissue (10-13).

Wound healing consists of serial events including inflammation, fibroblast proliferation,
10 secretion of ground substances, collagen production, angiogenesis, wound contraction and epithelialization. It can be divided in three phases; inflammatory, proliferative and remodeling phase (reviewed in (2)).

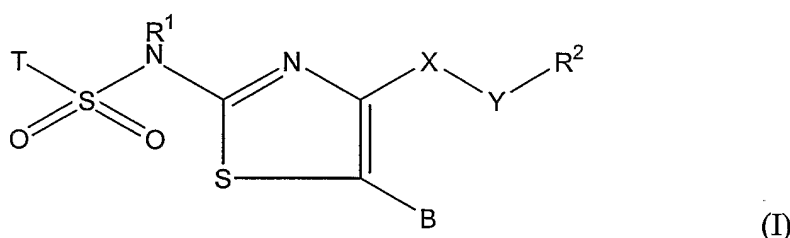
In surgical patients, treatment with glucocorticoids increases risk of wound infection
15 and delay healing of open wounds. It has been shown in animal models that restraint stress slows down cutaneous wound healing and increases susceptibility to bacterial infection during wound healing. These effects were reversed by treatment with the glucocorticoid receptor antagonist RU486 (14, 15). Glucocorticoids produce these effects by suppressing inflammation, decrease wound strength, inhibit wound
20 contracture and delay epithelialization (2). Glucocorticoids influence wound healing by interfering with production or action of cytokines and growth factors like IGF, TGF- β , EGF, KGF and PDGF (16-19). It has also been shown that glucocorticoids decrease collagen synthesis in rat and mouse skin in vivo and in rat and human fibroblasts (20).

25 WO 01/90090 discloses compounds of the formula (I) as defined hereinafter, which compounds inhibit the human 11 β -HSD1, and may be useful for treating disorders such as diabetes, obesity, glaucoma, osteoporosis, cognitive disorders and immune disorders. Other 11 β -HSD1 inhibitors are disclosed in e.g. WO 01/90091; WO 01/90092; WO 01/90093; WO 01/90094; WO 03/044000; WO 03/044009; WO 03/043999; and
30 Swedish patent application No. SE 0301504-7, filed on May 21, 2003. WO 02/072084 relates to glycyrrhetic acid derivatives, progesterone and progesterone derivatives as 11 β -HSD1 inhibitors for wound healing. However, the use of the 11 β -HSD1 inhibitors according to the present invention for wound healing has not previously been disclosed.

DISCLOSURE OF THE INVENTION

It has surprisingly been found that the present inhibitors of 11 β -HSD1 are useful for the
 5 promotion of wound healing. Consequently, in a first aspect this invention provides a
 method for promoting wound healing, said method comprising administering to a
 mammal, including man, in need of wound healing an effective amount of an inhibitor
 of 11 β -hydroxysteroid dehydrogenase type 1, wherein the inhibitor of 11 β -
 hydroxysteroid dehydrogenase type 1 is a compound of the formula (I):

10



wherein

15 T is an aryl ring or heteroaryl ring or aryl- C_2 -alkenyl ring, optionally independently
 substituted by $[\text{R}]_n$, wherein n is an integer 0-5, and R is hydrogen, aryl, heteroaryl, a
 heterocyclic ring, optionally halogenated C_{1-6} -alkyl, optionally halogenated C_{1-6} -alkoxy,
 C_{1-6} -alkylsulfonyl, carboxy, cyano, nitro, halogen, amine which is optionally mono- or
 di-substituted, amide which is optionally mono- or di-substituted, aryloxy, arylsulfonyl,
 20 arylamino, wherein aryl, heteroaryl and aryloxy residues and heterocyclic rings can
 further be optionally substituted in one or more positions independently of each other by
 C_{1-6} -acyl, C_{1-6} -alkylthio, cyano, nitro, hydrogen, halogen, optionally halogenated C_{1-6} -
 alkyl, optionally halogenated C_{1-6} -alkoxy, amide which is optionally mono- or di-
 substituted, (benzoylamino)methyl, carboxy, 2-thienylmethylamino or ({[4-(2-ethoxy-2-
 25 oxoethyl)-1,3-thiazol-2-yl]amino} carbonyl);

R^1 is hydrogen or C_{1-6} -alkyl;

X is CH_2 or CO ;

30

Y is CH₂, CO or a single bond;

B is hydrogen or C₁₋₆-alkyl;

- 5 R² is selected from C₁₋₆-alkyl, azido, arylthio, heteroarylthio, halogen, hydroxymethyl, 2-hydroxyethylaminomethyl, methylsulfonyloxymethyl, 3-oxo-4-morpholinolylmethylene, C₁₋₆-alkoxycarbonyl, and 5-methyl-1,3,4-oxadiazol-2-yl; NR³R⁴, wherein R³ and R⁴ are each independently selected from hydrogen, C₁₋₆-alkyl, optionally halogenated C₁₋₆-alkylsulfonyl, C₁₋₆-alkoxy, 2-methoxyethyl, 2-hydroxyethyl, 10 1-methylimidazolylsulfonyl, C₁₋₆-acyl, cyclohexylmethyl, cyclopropanecarbonyl, aryl, optionally halogenated arylsulfonyl, furylcarbonyl, tetrahydro-2-furanylmethyl, N-carbethoxypiperidyl and C₁₋₆-alkyl substituted with one or more aryl or heteroaryl, or NR³R⁴ represent together heterocyclic systems which can be imidazole, piperidine, pyrrolidine, piperazine, morpholine, oxazepine, oxazole, thiomorpholine, 1,1-15 dioxidothiomorpholine, 2-(3,4-dihydro-2(1H)isoquinoliny), (1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl, which heterocyclic systems can be optionally substituted by C₁₋₆-alkyl, C₁₋₆-acyl, hydroxy, oxo, t-butoxycarbonyl; OCONR³R⁴, wherein R³ and R⁴ are each independently selected from hydrogen, C₁₋₆-alkyl or form together morpholinyl;
- 20 R⁵O, wherein R⁵ is hydrogen, optionally halogenated C₁₋₆-alkyl, aryl, heteroaryl, C₁₋₆-acyl, C₁₋₆-alkylsulfonyl, arylcarbonyl, heteroarylcarbonyl, 2-carbomethoxyphenyl; and pharmaceutically acceptable salts, solvates, hydrates, geometrical isomers, tautomers, optical isomers, N-oxides and prodrug forms thereof.

- 25 It is preferred that:

T is selected from 5-chloro-1,3-dimethyl-1H-pyrazol-4-yl; 4-chloro-2,3,1-benzoxadiazolyl; 5-(dimethylamino)-1-naphthyl; 1-methylimidazol-4-yl; 1-naphthyl; 2-naphthyl; (E)-2-phenylethenyl; 8-quinoliny;

30 thienyl substituted with one or more of (benzoylamino)methyl, bromo, chloro, 3-isoxazolyl, 2-(methylsulfanyl)-4-pyrimidinyl, 1-methyl-5-(trifluoromethyl)pyrazol-3-yl, phenylsulfonyl, pyridyl;

phenyl substituted with one or more of acetylamino, 3-acetylaminophenyl, 3-acetylphenyl, benzeneamino, 1,3-benzodioxol-5-yl, 2-benzofuryl, benzylamino, 3,5-bis(trifluoromethyl)phenyl, bromo, butoxy, carboxy, chloro, 4-carboxyphenyl, 3-chloro-2-cyanophenoxy, 4-chlorophenyl, 5-chloro-2-thienyl, cyano, 3,4-dichlorophenyl, ({[4-
5 (2-ethoxy-2-oxoethyl)-1,3-thiazol-2-yl]amino} carbonyl), fluoro, 5-fluoro-2-methoxyphenyl, 2-furyl, hydrogen, iodo, isopropyl, methanesulfonyl, methoxy, methyl, 4-methyl-1-piperazinyl, 4-methyl-1-piperidinyl, 4-methylsulfanylphenyl, 5-methyl-2-thienyl, 4-morpholinyl, nitro, 3-nitrophenyl, phenoxy, phenyl, n-propyl, 4-pyridyl, 3-pyridylmethylamino, 1-pyrrolidinyl, 2-thienyl, 3-thienyl, 2-thienylmethylamino,
10 trifluoromethoxy, 4-trifluoromethoxyphenyl, and trifluoromethyl;

R¹ is hydrogen or methyl;

X is CH₂ or CO;

15

Y is CH₂, CO or a single bond;

B is hydrogen or methyl;

20 R² is selected from

n-propyl, azido, bromo, chloro, 2-pyridinylsulfanyl, 3-oxo-4-morpholinolinylmethylene, ethoxycarbonyl, 5-methyl-1,3,4-oxadiazol-2-yl;

NR³R⁴, wherein R³ and R⁴ are each independently selected from acetyl, 1,3-benzodioxol-5-ylmethyl, benzyl, 3-chloro-2-methylphenylsulfonyl, cyclohexylmethyl,
25 ethyl, 2-furylcarbonyl, 2-furylmethyl, hydrogen, 2-hydroxyethyl, 2-(1H-indol-3-yl)ethyl, isopropyl, methoxy, 2-methoxyethyl, methyl, 4-(1-methylimidazolyl)sulfonyl, methylsulfonyl, phenyl, propyl, trifluoromethylsulfonyl; or

NR³R⁴ represent together 4-acetylpiperazinyl, 4-t-butoxycarbonylpiperazinyl, 2-(3,4-dihydro-2(1H)isoquinolinyll), (2R,6S)-2,6-dimethylmorpholinyl, (2R)-2,4-dimethyl-1-piperazinyl, 2-hydroxy-3-oxomorpholinyl, imidazolyl, 2-methyl-3-oxomorpholinyl, 4-methyl-2-oxopiperazinyl, 4-methylpiperazinyl, morpholinyl, (1S,4S)-2-oxa-5-aza-bicyclo[2.2.1]hept-5-yl, 2-oxoimidazolinyll, 3-oxomorpholinyl, 3-oxo-1,4-oxazepinyll, 2-

30

oxooxazoliny, piperazinyl; piperidinyl; pyrrolidinyl; pyrrolidonyl, thiomorpholinyl;
1,1-dioxido-thiomorpholinyl;

OCNR³R⁴, wherein R³ and R⁴ are each independently selected from ethyl, hydrogen
or form together morpholinyl;

- 5 R⁵O, wherein R⁵ is selected from acetyl, benzoyl, benzyl, ethyl, 2-fluoroethyl, 2-furylcarbonyl, hydrogen, isobutyryl, isopropyl, methyl, 2-carbomethoxyphenyl, methylsulfonyl, phenyl, propionyl, 3-pyridinyl, and 2,2,2-trifluoroethyl.

The following compounds are especially preferred:

10

ethyl (2-{{(2,4-dichloro-5-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl 2-(2-{{(4-chlorophenyl)sulfonyl}amino}-1,3-thiazole-4-yl)acetate,
ethyl 2-(2-{{(4-chloro-2,5-dimethylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,

15

ethyl 2-(2-{{(2,4-difluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl 2-(2-{{(4-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl 2-(2-{{(2,5-dichloro-3-thienyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(2-chlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,

20

ethyl 2-{2-[[1,1'-biphenyl]-4-ylsulfonyl]amino}-1,3-thiazol-4-yl} acetate,
ethyl 2-(2-{{(3-bromophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(4-nitrophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(4-methoxyphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,

25

ethyl (2-{{(3-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(3-chlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(4-fluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(3-fluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl {2-[(phenylsulfonyl)amino]-1,3-thiazol-4-yl} acetate,

30

ethyl (2-{{(4-isopropylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl [2-(3-{{(4-(2-ethoxy-2-oxoethyl)-1,3-thiazol-2-yl}amino} carbonyl)phenyl)sulfonyl}amino)-1,3-thiazol-4-yl]acetate,

ethyl [2-({[4-({[4-(2-ethoxy-2-oxoethyl)-1,3-thiazol-2-yl]amino} carbonyl)phenyl]sulfonyl} amino)-1,3-thiazol-4-yl]acetate,
ethyl (2-{[(2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl [2-({[2-(trifluoromethyl)phenyl]sulfonyl} amino)-1,3-thiazol-4-yl]acetate,
ethyl [2-({[3-(trifluoromethyl)phenyl]sulfonyl} amino)-1,3-thiazol-4-yl]acetate,
ethyl [2-({[4-(trifluoromethyl)phenyl]sulfonyl} amino)-1,3-thiazol-4-yl]acetate,
ethyl 2-(2-{[(4-bromophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(2-nitrophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(2,4-dichloro-6-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(2,4,6-trichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(2,4-dichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(5-fluoro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(4-propylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(2-methoxy-4-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(3,5-dichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl [2-({[4-(3-chloro-2-cyanophenoxy)phenyl]sulfonyl} amino)-1,3-thiazol-4-yl]acetate,
ethyl (2-{[(3,4-dichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(4-butoxyphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(4-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl [2-({[4-(acetylamino)phenyl]sulfonyl} amino)-1,3-thiazol-4-yl]acetate,
ethyl {2-[(8-quinoliny)sulfonyl]amino}-1,3-thiazol-4-yl} acetate,
ethyl (2-{[(3,4-dimethoxyphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(4-iodophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(3-chloro-4-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl [2-({[5-(dimethylamino)-1-naphthyl]sulfonyl} amino)-1,3-thiazol-4-yl]acetate,
ethyl (2-{[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(5-bromo-2-methoxyphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(2,5-dimethoxyphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl {2-[(2-naphthyl)sulfonyl]amino}-1,3-thiazol-4-yl} acetate,
ethyl {2-[(mesityl)sulfonyl]amino}-1,3-thiazol-4-yl} acetate,
ethyl (2-{[(3-bromo-5-chloro-2-thienyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,

- ethyl {2-[(5-[(benzoylamino)methyl]-2-thienyl)sulfonyl]amino}-1,3-thiazol-4-yl} acetate,
- ethyl {2-[(5-[1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl]-2-thienyl)sulfonyl]amino}-1,3-thiazol-4-yl} acetate,
- 5 ethyl (2-{[(4-cyanophenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- ethyl {2-[(5-[2-(methylsulfonyl)-4-pyrimidinyl]-2-thienyl)sulfonyl]amino}-1,3-thiazol-4-yl} acetate,
- ethyl (2-{[(3-cyanophenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- ethyl (2-{[(2,4,5-trichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- 10 ethyl [2-({[(E)-2-phenylethenyl)sulfonyl]amino}-1,3-thiazol-4-yl] acetate,
- ethyl (2-{[(2,3,4-trichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- ethyl (2-{[(4-bromo-2,5-difluorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl] acetate,
- ethyl [2-({[4-(trifluoromethoxy)phenyl)sulfonyl]amino}-1,3-thiazol-4-yl] acetate,
- ethyl (2-{[(2,3-dichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- 15 ethyl (2-{[(2-bromophenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- ethyl (2-{[(4,5-dichloro-2-thienyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- ethyl [2-({[4-(phenylsulfonyl)-2-thienyl]sulfonyl]amino}-1,3-thiazol-4-yl] acetate,
- ethyl [2-({[5-(phenylsulfonyl)-2-thienyl]sulfonyl]amino}-1,3-thiazol-4-yl] acetate,
- ethyl (2-{[(2,6-dichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- 20 ethyl (2-{[(2-cyanophenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- ethyl (2-({[4-(acetylamino)-3-chlorophenyl]sulfonyl]amino}-1,3-thiazol-4-yl] acetate,
- ethyl (2-{[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- 25 ethyl (2-{[(3-methoxyphenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- ethyl (2-{[(4-bromo-5-chloro-2-thienyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- ethyl 2-{2-[(1-naphthylsulfonyl]amino}-1,3-thiazol-4-yl} acetate,
- ethyl (2-{[(2,5-dichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- ethyl (2-{[(4-methanesulfonylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- 30 ethyl (2-{[(2-methanesulfonylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- ethyl (2-{[(4-bromo-2-fluorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,
- ethyl (2-{[(2-methyl-4-trifluoromethoxyphenyl)sulfonyl]amino}-1,3-thiazol-4-yl) acetate,

- ethyl (2-{{(2,3,4-trifluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(4-chloro-2,3,1-benzoxadiazolyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(2,4,6-trifluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
5 ethyl (2-{{(5-carboxy-4-chloro-2-fluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(2-(5-chlorothieryl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(2-chloro-4-fluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(2-(5-(3-isoxazolo)thienyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
10 ethyl (2-{{(4-bromo-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(4-phenoxyphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(4-chloro-2,6-dimethylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(2-methyl-4-trifluoromethoxyphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
15 ethyl (2-{{(2,4-bis(trifluoromethyl)phenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl 2-{2-[[{(3-chloro-2-methylphenyl)sulfonyl}(methyl)amino]-1,3-thiazol-4-yl}acetate,
ethyl oxo(2-{{(4-propylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
20 ethyl (2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)(oxo)acetate,
ethyl oxo(2-{{(2,4,6-trichlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl {2-[[{(1,1'-biphenyl)-4-ylsulfonyl}amino]-1,3-thiazol-4-yl}(oxo)acetate,
ethyl (2-{{(2,4-dichloro-6-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)(oxo)acetate,
25 2-(2-{{(4-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetic acid,
2-(2-{{(2,5-dichloro-3-thienyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetic acid,
(2-{{(2-chlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetic acid,
2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetic acid,
30 isopropyl 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
phenyl 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
methyl (2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,

- methyl {2-[(1,1'-biphenyl)-4-ylsulfonyl]amino}-5-methyl-1,3-thiazol-4-yl} acetate,
- methyl (2-{[(4-chlorophenyl)sulfonyl]amino}-5-methyl-1,3-thiazol-4-yl)acetate,
- methyl (2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-5-methyl-1,3-thiazol-4-yl)acetate,
- 5 methyl [2-({[4-(3-chloro-2-cyanophenoxy)phenyl]sulfonyl}amino)-5-methyl-1,3-thiazol-4-yl]acetate,
- methyl (5-methyl-2-{[(4-propylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
- methyl (5-methyl-2-{[(2,4,6-trichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
- 10 methyl (2-{[(2,4-dichloro-6-methylphenyl)sulfonyl]amino}-5-methyl-1,3-thiazol-4-yl)acetate,
- N-(2-methoxyethyl)-2-(2-{[(4-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetamide,
- 15 2-(2-{[(2,5-dichloro-3-thienyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N-methylacetamide,
- N-(1,3-benzodioxol-5-ylmethyl)-2-{2-[(1-naphthylsulfonyl)amino]-1,3-thiazol-4-yl}acetamide,
- N-(2-furylmethyl)-2-{2-[(1-naphthylsulfonyl)amino]-1,3-thiazol-4-yl}acetamide,
- 20 2-(2-{[(2,4-difluorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N-ethylacetamide,
- N-isopropyl-2-{2-[(1-naphthylsulfonyl)amino]-1,3-thiazol-4-yl}acetamide,
- N-[2-(1H-indol-3-yl)ethyl]-2-{2-[(1-naphthylsulfonyl)amino]-1,3-thiazol-4-yl}acetamide,
- N-(cyclohexylmethyl)-2-{2-[(phenylsulfonyl)amino]-1,3-thiazol-4-yl}acetamide,
- 25 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N-methylacetamide,
- 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N-ethylacetamide,
- 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N-phenylacetamide,
- 30 2-(2-{[(4-chlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N-(2-furylmethyl)acetamide,
- 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetamide,

- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N,N-diethylacetamide,
- 2-{2-[[1,1'-biphenyl]-4-ylsulfonyl]amino}-1,3-thiazol-4-yl)-N,N-diethylacetamide,
- 5 N,N-diethyl-2-(2-{{(4-propylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetamide,
- 2-(2-{{(2,4-dichloro-6-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N,N-diethylacetamide,
- N,N-diethyl-2-(2-{{(2,4,6-trichlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetamide,
- 10 2-{2-[[1,1'-biphenyl]-4-ylsulfonyl]amino}-1,3-thiazol-4-yl)-N,N-diisopropylacetamide,
- N,N-diisopropyl-2-(2-{{(4-propylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetamide,
- 2-(2-{{(2,4-dichloro-6-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N,N-diisopropylacetamide,
- 15 N,N-diisopropyl-2-(2-{{(2,4,6-trichlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetamide,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N,N-diisopropylacetamide,
- 20 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N,N-dipropylacetamide,
- N-benzyl-2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-ethylacetamide,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N,N-dimethylacetamide,
- 25 3-chloro-N-{4-[2-(3,4-dihydro-2(1H)-isoquinolinyl)-2-oxoethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-methyl-N-phenylacetamide,
- 30 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-isopropyl-N-methylacetamide,
- 2-{2-[[1,1'-biphenyl]-4-ylsulfonyl]amino}-1,3-thiazol-4-yl)-N-isopropyl-N-methylacetamide,

- N-ethyl-N-methyl-2-(2-{{(2,4,6-trichlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetamide,
- 2-(2-{{(2,4-dichloro-6-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-ethyl-N-methylacetamide,
- 5 N-ethyl-N-methyl-2-(2-{{(4-propylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetamide,
- 2-{2-{{(1,1'-biphenyl)-4-ylsulfonyl}amino}-1,3-thiazol-4-yl}-N-ethyl-N-methylacetamide,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-ethyl-N-methylacetamide,
- 10 3-chloro-2-methyl-N-{4-[2-oxo-2-(1-pyrrolidiny)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 3-chloro-2-methyl-N-{4-[2-oxo-2-(1-piperidiny)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 15 N-{4-[2-oxo-2-(1-piperidiny)ethyl]-1,3-thiazol-2-yl}[1,1'-biphenyl]-4-sulfonamide,
- N-{4-[2-oxo-2-(1-piperidiny)ethyl]-1,3-thiazol-2-yl}-4-propylbenzenesulfonamide,
- 2,4-dichloro-6-methyl-N-{4-[2-oxo-2-(1-piperidiny)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 20 2,4,6-trichloro-N-{4-[2-oxo-2-(1-piperidiny)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 3-chloro-2-methyl-N-{4-[2-(4-morpholiny)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 25 2,4,6-trichloro-N-{4-[2-(4-morpholiny)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 2,4-dichloro-6-methyl-N-{4-[2-(4-morpholiny)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- N-{4-[2-(4-morpholiny)-2-oxoethyl]-1,3-thiazol-2-yl}[1,1'-biphenyl]-4-sulfonamide,
- 30 N-{4-[2-(4-morpholiny)-2-oxoethyl]-1,3-thiazol-2-yl}-4-propylbenzenesulfonamide,

- 2,4-dichloro-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-chloro-2,6-dimethyl-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 5 N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}-4-phenoxybenzenesulfonamide,
- 2-methyl-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}-4-(trifluoromethoxy)benzenesulfonamide,
- N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}-2,4-
- 10 bis(trifluoromethyl)benzenesulfonamide,
- 4-bromo-2-methyl-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(2-furyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 15 4-(5-fluoro-2-methoxyphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(5-methyl-2-thienyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(3-acetylphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 20 4-(4-trifluoromethoxyphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(3,4-dichlorophenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 25 4-(3,4-methylenedioxyphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(5-chloro-2-thienyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(4-pyridyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 30 4-(3-acetylaminophenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,

- 4-(3-thienyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(2-thienyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 5 4-(4-carboxyphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(4-methylsulfanylphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(3,5-bis(trifluoromethyl)phenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 10 4-(4-chlorophenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(3-nitrophenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 15 4-(2-benzofuryl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(1-pyrrolidino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(4-methyl-1-piperidino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 20 4-(benzeneamino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(benzylamino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 25 4-(2-thienylmethylamino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(4-morpholinyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(4-methyl-1-piperazinyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 30 4-(3-pyridylmethylamino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,

- 2,4-dichloro-6-methyl-N-{5-methyl-4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
N-{5-methyl-4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}[1,1'-biphenyl]-4-sulfonamide,
5 2,4,6-trichloro-N-{5-methyl-4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
3-chloro-2-methyl-N-{5-methyl-4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
3-chloro-N-(4-{2-[(2R,6S)-2,6-dimethylmorpholinyl]-2-oxoethyl}-1,3-thiazol-2-yl)-2-methylbenzenesulfonamide,
10 3-chloro-2-methyl-N-(4-{2-[(1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl]-2-oxoethyl}-1,3-thiazol-2-yl)benzenesulfonamide,
3-chloro-2-methyl-N-{4-[2-oxo-2-(4-thiomorpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
15 N-{4-[2-oxo-2-(4-thiomorpholinyl)ethyl]-1,3-thiazol-2-yl}[1,1'-biphenyl]-4-sulfonamide,
N-{4-[2-oxo-2-(4-thiomorpholinyl)ethyl]-1,3-thiazol-2-yl}-4-propylbenzenesulfonamide,
2,4-dichloro-6-methyl-N-{4-[2-oxo-2-(4-thiomorpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
20 2,4,6-trichloro-N-{4-[2-oxo-2-(4-thiomorpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
N-{4-[2-(1,1-dioxido-4-thiomorpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}-4-propylbenzenesulfonamide,
25 tert-butyl 4-[(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetyl]-1-piperazinecarboxylate,
4-acetyl-(4-[(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetyl])-1-piperazine,
4-[(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetyl]-1-piperazine trifluoroacetate,
30 3-chloro-2-methyl-N-{4-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide hydrochloride,

- 2-methyl-N-{4-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-1,3-thiazol-2-yl}-4-(trifluoromethoxy)benzenesulfonamide,
2,4-dichloro-6-methyl-N-{4-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
5 2,4-dichloro-N-{4-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
3-chloro-N-(4-{2-[(2R)-2,4-dimethylpiperazinyl]-2-oxoethyl}-1,3-thiazol-2-yl)-2-methylbenzenesulfonamide,
2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N-methoxy-N-methylacetamide,
10 3-chloro-2-methyl-N-[4-(2-oxopentyl)-1,3-thiazol-2-yl]benzenesulfonamide,
4-chloro-N-[4-(2-hydroxyethyl)-1,3-thiazol-2-yl]benzenesulfonamide,
3-chloro-N-[4-(2-hydroxyethyl)-1,3-thiazol-2-yl]-2-methylbenzenesulfonamide,
3-chloro-N-[4-(2-ethoxyethyl)-1,3-thiazol-2-yl]-2-methylbenzenesulfonamide,
15 3-chloro-N-[4-(2-isopropoxyethyl)-1,3-thiazol-2-yl]-2-methylbenzenesulfonamide,
N-{4-[2-(benzyloxy)ethyl]-1,3-thiazol-2-yl}-3-chloro-2-methylbenzenesulfonamide,
3-chloro-N-[4-(2-methoxyethyl)-1,3-thiazol-2-yl]-2-methylbenzenesulfonamide,
20 3-chloro-N-{4-[2-(2-fluoroethoxy)ethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide,
3-chloro-2-methyl-N-{4-[2-(2,2,2-trifluoroethoxy)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
3-chloro-2-methyl-N-{4-[2-(2-pyridinylsulfanyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
25 3-chloro-2-methyl-N-{4-[2-(3-pyridinyloxy)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
3-chloro-2-methyl-N-{4-[2-methylsalicylethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
30 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)ethyl methanesulfonate,
2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)ethyl acetate,

- 2-(2-[[[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl]ethyl
propionate,
- 2-(2-[[[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl]ethyl 2-
methylpropanoate,
- 5 2-(2-[[[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl]ethyl 2-
furoate,
- 2-(2-[[[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl]ethyl
benzoate,
- 2-(2-[[[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl]ethyl 4-
10 morpholinecarboxylate,
- 2-(2-[[[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl]ethyl
diethylcarbamate,
- 2-(2-[[[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl]ethyl
ethylcarbamate,
- 15 N-[4-(2-azidoethyl)-1,3-thiazol-2-yl]-3-chloro-2-methylbenzenesulfonamide,
N-[4-(2-aminoethyl)-1,3-thiazol-2-yl]-3-chloro-2-methylbenzenesulfonamide
hydrochloride,
- 4-chloro-N-{4-[2-(diethylamino)ethyl]-1,3-thiazol-2-yl} benzenesulfonamide
hydrochloride,
- 20 3-chloro-N-{4-[2-(diethylamino)ethyl]-1,3-thiazol-2-yl}-2-
methylbenzenesulfonamide hydrochloride,
- 3-chloro-N-{4-[2-(1-imidazolyl)ethyl]-1,3-thiazol-2-yl}-2-
methylbenzenesulfonamide hydrochloride,
- 3-chloro-2-methyl-N-{4-[2-(4-methyl-1-piperazinyl)ethyl]-1,3-thiazol-2-
25 yl} benzenesulfonamide dihydrochloride,
- 3-chloro-2-methyl-N-{4-[2-(4-morpholinyl)ethyl]-1,3-thiazol-2-
yl} benzenesulfonamide hydrochloride,
- 3-chloro-2-methyl-N-{4-[2-(4-morpholinyl)methyl]-1,3-thiazol-2-
yl} benzenesulfonamide hydrochloride,
- 30 2,4,6-trichloro-N-{4-[2-(4-morpholinyl)ethyl]-1,3-thiazol-2-
yl} benzenesulfonamide hydrochloride,
- 2,4-dichloro-N-{4-[2-(4-morpholinyl)ethyl]-1,3-thiazol-2-yl} benzenesulfonamide
hydrochloride,

- 2,4-dichloro-6-methyl-N-{4-[2-(4-morpholinyl)ethyl]-1,3-thiazol-2-yl} benzenesulfonamide hydrochloride,
N-{4-[2-(4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-4-propylbenzenesulfonamide
hydrochloride,
5 3-chloro-N-{4-[2-(ethylamino)ethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide,
3-chloro-N-(4-{2-[(2-hydroxyethyl)amino]ethyl}-1,3-thiazol-2-yl)-2-methylbenzenesulfonamide,
N-[2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)ethyl]-N-ethylacetamide,
10 3-chloro-2-methyl-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl} benzenesulfonamide,
3-chloro-N-{4-[2-(2-hydroxy-3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide,
15 2,4-dichloro-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl} benzenesulfonamide,
2,4-dichloro-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-6-methylbenzenesulfonamide,
N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-2,4,6-trichlorobenzenesulfonamide,
20 4,5-dichloro-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-2-thienylsulfonamide,
N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-4-phenoxybenzenesulfonamide,
25 3-fluoro-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl} benzenesulfonamide,
N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-5-(2-pyridyl)-2-thienylsulfonamide,
4-acetylamino-3-chloro-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl} benzenesulfonamide,
30 N-{4-[(3-oxo-4-morpholinyl)methyl]-1,3-thiazol-2-yl}-3-chloro-2-methylbenzenesulfonamide,

- N-{4-[3-(3-oxo-4-morpholinyl)propyl]-1,3-thiazol-2-yl}-3-chloro-2-methylbenzenesulfonamide,
- N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl},N-methyl-3-chloro-2-methylbenzenesulfonamide,
- 5 3-chloro-2-methyl-N-{4-[2-(2-methyl-3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- N-{4-[2-(acetylamino)ethyl]-1,3-thiazol-2-yl}-3-chloro-2-methylbenzenesulfonamide,
- 3-chloro-2-methyl-N-{4-[2-(4-(3-oxo-1,4-oxazepinyl))ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 10 3-chloro-2-methyl-N-{4-[2-(1-pyrrolidonyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 3-chloro-2-methyl-N-{4-[2-(1-(2-oxoimidazoliny))ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 15 3-chloro-2-methyl-N-{4-[2-(1-(2-oxooxazoliny))ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 3-chloro-N-{4-[2-(N-(2-furylcarbonyl),N-2-hydroxyethylamino)ethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide, hydrochloride,
- 3-chloro-2-methyl-N-{4-[2-(4-methyl-2-oxopiperazinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 20 3-chloro-2-methyl-N-{4-[2-(methylsulfonylamino)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 3-chloro-2-methyl-N-{4-[2-(N-methyl,N-methylsulfonylamino)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 25 3-chloro-2-methyl-N-{4-[2-(trifluoromethylsulfonylamino)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 3-chloro-2-methyl-N-{4-[2-(N-methyl,N-trifluoromethylsulfonylamino)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 3-chloro-2-methyl-N-{4-[2-(4-(1-methylimidazolyl)sulfonylamino)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 30 3-chloro-N-{4-[2-(N-(3-chloro-2-methylphenylsulfonyl),N-methylamino)ethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide,
- N-[4-(2-bromoethyl)-1,3-thiazol-2-yl]-3-chloro-2-methylbenzenesulfonamide,

3-chloro-N-[4-(2-chloroethyl)-1,3-thiazol-2-yl]-2-methylbenzenesulfonamide,
3-chloro-2-methyl-N-{4-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-1,3-thiazol-2-yl}
benzenesulfonamide,
3-chloro-N-{4-[2-(ethoxycarbonyl)ethyl]-1,3-thiazol-2-yl}-2-
5 methylbenzenesulfonamide.

In one aspect of the invention, the said method is a method for the treatment or prophylaxis of a medical condition involving delayed or impaired wound healing. Examples of such medical conditions are diabetes, and conditions caused by treatment
10 with steroids, in particular glucocorticoids. The method according to the invention is also intended for the promotion of wound healing in chronic wounds, such as diabetic ulcers, venous ulcers or pressure ulcers.

The compounds referred to above may also be used in the manufacture of a medicament
15 for promoting wound healing, e.g. for the treatment or prophylaxis of a medical condition involving delayed or impaired wound healing. Examples of such medical conditions are diabetes, and conditions caused by treatment with steroids, in particular glucocorticoids. The compounds referred to above may also be used for the promotion of wound healing in chronic wounds, such as diabetic ulcers, venous ulcers or pressure
20 ulcers.

The various terms used, separately and in combinations, in the above definition of the compounds having the general formula (I) will be explained.

25 The term "aryl" in the present description is intended to include aromatic rings (monocyclic or bicyclic) having from 6 to 10 ring carbon atoms, such as phenyl (Ph) and naphthyl, which optionally may be substituted by C₁₋₆-alkyl. Examples of substituted aryl groups are benzyl and 2-methylphenyl.

30 The term "heteroaryl" means in the present description a monocyclic, bi- or tricyclic aromatic ring system (only one ring need to be aromatic) having from 5 to 14, preferably 5 to 10 ring atoms such as 5, 6, 7, 8, 9 or 10 ring atoms (mono- or bicyclic), in which one or more of the ring atoms are other than carbon, such as nitrogen, sulfur,

oxygen and selenium. Examples of such heteroaryl rings are pyrrole, imidazole, thiophene, furan, thiazole, isothiazole, thiadiazole, oxazole, isoxazole, oxadiazole, pyridine, pyrazine, pyrimidine, pyridazine, pyrazole, triazole, tetrazole, chroman, isochroman, quinoline, quinoxaline, isoquinoline, phthalazine, cinnoline, quinazoline, indole, isoindole, indoline, isoindoline, benzothiophene, benzofuran, isobenzofuran, benzoxazole, 2,1,3-benzoxadiazole, benzothiazole, 2,1,3-benzothiazole, 2,1,3-benzoselenadiazole, benzimidazole, indazole, benzodioxane, indane, 1,2,3,4-tetrahydroquinoline, 3,4-dihydro-2*H*-1,4-benzoxazine, 1,5-naphthyridine, 1,8-naphthyridine, acridine, fenazine and xanthene. Examples of monocyclic heteroaryl rings are pyrrole, imidazole, thiophene, furan, thiazole, isothiazole, thiadiazole, oxazole, isoxazole, oxadiazole, pyridine, pyrazine, pyrimidine, pyridazine, pyrazole, triazole, and tetrazole.

The term "heterocyclic" in the present description is intended to include unsaturated as well as partially and fully saturated mono-, bi- and tricyclic rings having from 4 to 14, preferably 4 to 10 ring atoms, such as, for example, the heteroaryl groups mentioned above as well as the corresponding partially saturated or fully saturated heterocyclic rings. Exemplary saturated heterocyclic rings are azetidine, pyrrolidine, piperidine, piperazine, morpholine, thiomorpholine and 1,4-oxazepane.

C₁₋₆-alkyl in the compound of formula (I) according to the present application, which may be straight or branched, is preferably C₁₋₄-alkyl. Exemplary alkyl groups include methyl, ethyl, propyl, isopropyl, butyl, sec-butyl, tert-butyl, pentyl, isopentyl, hexyl, and isoheptyl. For parts of the range "C₁₋₆-alkyl" all subgroups thereof are contemplated such as C₁₋₅-alkyl, C₁₋₄-alkyl, C₂₋₆-alkyl, C₂₋₅-alkyl, C₂₋₄-alkyl, C₂₋₃-alkyl, C₃₋₆-alkyl, C₄₋₅-alkyl, etc.

C₁₋₆-alkoxy, in the compound of formula (I) according to the present application may be straight or branched, is preferably C₁₋₄-alkoxy. Exemplary alkoxy groups include methoxy, ethoxy, propoxy, isopropoxy, butoxy, sec-butoxy, tert-butoxy, pentyloxy, isopentyloxy, hexyloxy, and isoheptyloxy. For parts of the range "C₁₋₆-alkoxy" all subgroups thereof are contemplated such as C₁₋₅-alkoxy, C₁₋₄-alkoxy, C₂₋₆-alkoxy, C₂₋₅-alkoxy, C₂₋₄-alkoxy, C₂₋₃-alkoxy, C₃₋₆-alkoxy, C₄₋₅-alkoxy, etc.

C₁₋₆-acyl, in the compound of formula (I) according to the present application may be saturated or unsaturated and is preferably C₁₋₄-acyl. Exemplary acyl groups include formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl, butenoyl (e.g. 3-
5 butenoyl), hexenoyl (e.g. 5-hexenoyl). For parts of the range "C₁₋₆-acyl" all subgroups thereof are contemplated such as C₁₋₅-acyl, C₁₋₄-acyl, C₂₋₆-acyl, C₂₋₅-acyl, C₂₋₄-acyl, C₂₋₃-acyl, C₃₋₆-acyl, C₄₋₅-acyl, etc.

C₂₋₆-alkenyl in the compound of formula (I) according to the present application, which
10 may be straight, branched or cyclic, is preferably C₂₋₄-alkenyl. Exemplary alkenyl groups include vinyl, 1-propenyl, 2-propenyl, isopropenyl, 1-butenyl, 2-butenyl, 1-pentenyl, 2-pentenyl, 1-hexenyl, and 2-hexenyl. For parts of the range "C₂₋₆-alkenyl" all subgroups thereof are contemplated such as C₂₋₅-alkenyl, C₂₋₄-alkenyl, C₂₋₃-alkenyl, C₃₋₆-alkenyl, C₄₋₅-alkenyl, etc.

15

The term "halogen" in the present description is intended to include fluorine, chlorine, bromine and iodine.

The term "sulfanyl" in the present description means a thio group.

20

With the expression mono- or di-substituted is meant in the present description that the functionalities in question may be substituted with independently H, C₁₋₆-acyl, C₁₋₆-alkenyl, C₁₋₆-(cyclo)alkyl, aryl, pyridylmethyl, or heterocyclic rings e.g. azetidine, pyrrolidine, piperidine, piperazine, morpholine and thiomorpholine, which heterocyclic
25 rings optionally may be substituted with C₁₋₆-alkyl. With the expression "optionally mono- or disubstituted" is meant in the present description that the functionalities in question may also be substituted with independently hydrogen.

Combinations of substituents and variables envisioned by this invention are only those
30 that result in the formation of stable compounds. The term "stable", as used herein, refers to compounds which possess stability sufficient to allow manufacture and which maintains the integrity of the compound for a sufficient period of time to be useful for

the purposes detailed herein (e.g., therapeutic administration to a subject for the treatment of disease, 11- β -HSD1 inhibition, 11- β -HSD1-mediated disease).

The term "prodrug forms" in the present description means a pharmacologically acceptable derivative, such as an ester or an amide, which derivative is biotransformed in the body to form the active drug (see Goodman and Gilman's, The Pharmacological basis of Therapeutics, 8th ed., McGraw-Hill, Int. Ed. 1992, "Biotransformation of Drugs, p. 13-15).

"Pharmaceutically acceptable" means in the present description being useful in preparing a pharmaceutical composition that is generally safe, non-toxic and neither biologically nor otherwise undesirable and includes being useful for veterinary use as well as human pharmaceutical use.

"Pharmaceutically acceptable salts" mean in the present description salts which are pharmaceutically acceptable, as defined above, and which possess the desired pharmacological activity. Such salts include acid addition salts formed with organic and inorganic acids, such as hydrogen chloride, hydrogen bromide, hydrogen iodide, sulfuric acid, phosphoric acid, acetic acid, glycolic acid, maleic acid, malonic acid, oxalic acid, methanesulfonic acid, trifluoroacetic acid, fumaric acid, succinic acid, tartaric acid, citric acid, benzoic acid, ascorbic acid and the like. Base addition salts may be formed with organic and inorganic bases, such as sodium, ammonia, potassium, calcium, ethanolamine, diethanolamine, N-methylglucamine, choline and the like.

The compounds of formula (I) can be prepared according to the methods described in WO 01/90090.

For use according to the invention, the compounds of formula (I) can preferably be topically administered. However, the compounds could also be administered by other routes, for instance orally, intraperitoneally, intraarticularly, intracranially, intradermally, intramuscularly, intraocularly, intrathecally, intravenously, subcutaneously.

EXAMPLES

EXAMPLE 1

5

Diabetic KKAy mice underwent surgery during anesthesia whereby a catheter was inserted in the jugularis vein. Oral treatment twice daily (200 mg/kg/day) with the 11 β -HSD1 inhibitor BVT.2733 (3-Chloro-2-methyl-N-{4-[2-oxo-2-(1-piperazinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide; the trifluoroacetate of this compound is disclosed as Example 172A in WO 01/90090), or vehicle started 4-6 days later and continued for 3.5 days.

Advantageous effects on wound healing of the surgical wounds were observed during treatment. In BVT.2733 treated mice, less complication were observed in and around the wound area as compared to control mice. Examples of advantageous effects were less pus in the wound, as well as better wound strength. 58 % of the vehicle treated animals showed complications during treatment period whereas complications were present in only 24 % of the BVT.2733 treated animals.

20

EXAMPLE 2

(a)

Advantageous effects of 11 β -HSD1 inhibitors (e.g. BVT.2733) on wound healing are confirmed in diabetic KKA^y mice employing the excisional wound-healing model. 1 cm full-thickness wounds, including the panniculus carnosus muscle, are cut with a scalpel on the back of the mice. Mice are treated with BVT.2733 for 5 days. On day 2 and 9 of treatment wounds are harvested, embedded and sectioned. Histological staining of the sections with hematoxylin/eosin are made to determine degree of re-epithelialization and immunostaining against the von Willebrand factor to determine revascularisation.

30

(b)

Advantageous effects of 11 β -HSD1 inhibitors are confirmed in *in vitro* studies.

Proliferation of human keratinocytes and fibroblasts, which are important cell types in the wound healing process, are studied after incubation with the 11 β -HSD1 inhibitor.

5

(c)

Effects on wound healing after treatment with 11 β -HSD1 inhibitors are also studied in wounds on explants from human breast skin. The proliferative effect of the substance and the effect on re-epithelialization are determined.

10

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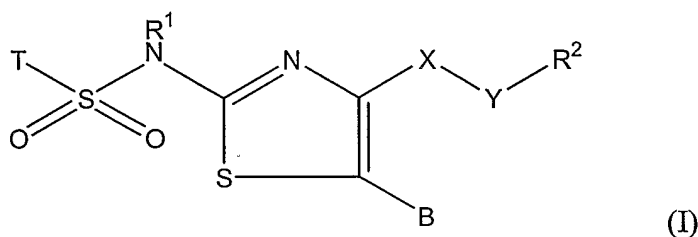
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Claims

1. A method for promoting wound healing, said method comprising administering to a mammal, including man, in need of wound healing an effective amount of an inhibitor of 11- β -hydroxysteroid dehydrogenase type 1, wherein the inhibitor of 11- β -hydroxysteroid dehydrogenase type 1 is a compound of the formula (I):



10 wherein

T is an aryl ring or heteroaryl ring or aryl-C₂-alkenyl ring, optionally independently substituted by [R]_n, wherein n is an integer 0-5, and R is hydrogen, aryl, heteroaryl, a heterocyclic ring, optionally halogenated C₁₋₆-alkyl, optionally halogenated C₁₋₆-alkoxy, C₁₋₆-alkylsulfonyl, carboxy, cyano, nitro, halogen, amine which is optionally mono- or di-substituted, amide which is optionally mono- or di-substituted, aryloxy, arylsulfonyl, arylamino, wherein aryl, heteroaryl and aryloxy residues and heterocyclic rings can further be optionally substituted in one or more positions independently of each other by C₁₋₆-acyl, C₁₋₆-alkylthio, cyano, nitro, hydrogen, halogen, optionally halogenated C₁₋₆-alkyl, optionally halogenated C₁₋₆-alkoxy, amide which is optionally mono- or di-substituted, (benzoylamino)methyl, carboxy, 2-thienylmethylamino or ({[4-(2-ethoxy-2-oxoethyl)-1,3-thiazol-2-yl]amino} carbonyl);

R¹ is hydrogen or C₁₋₆-alkyl;

X is CH₂ or CO;

Y is CH₂, CO or a single bond;

B is hydrogen or C₁₋₆-alkyl;

R^2 is selected from C_{1-6} -alkyl, azido, arylthio, heteroarylthio, halogen, hydroxymethyl, 2-hydroxyethylaminomethyl, methylsulfonyloxymethyl, 3-oxo-4-morpholinolinylmethylene, C_{1-6} -alkoxycarbonyl, and 5-methyl-1,3,4-oxadiazol-2-yl;

5 NR^3R^4 , wherein R^3 and R^4 are each independently selected from hydrogen, C_{1-6} -alkyl, optionally halogenated C_{1-6} -alkylsulfonyl, C_{1-6} -alkoxy, 2-methoxyethyl, 2-hydroxyethyl, 1-methylimidazolylsulfonyl, C_{1-6} -acyl, cyclohexylmethyl, cyclopropanecarbonyl, aryl, optionally halogenated arylsulfonyl, furylcarbonyl, tetrahydro-2-furanylmethyl, N-carbethoxypiperidyl and C_{1-6} -alkyl substituted with one or more aryl or heteroaryl, or

10 NR^3R^4 represent together heterocyclic systems which can be imidazole, piperidine, pyrrolidine, piperazine, morpholine, oxazepine, oxazole, thiomorpholine, 1,1-dioxidothiomorpholine, 2-(3,4-dihydro-2(1H)isoquinoliny), (1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl, which heterocyclic systems can be optionally substituted by C_{1-6} -alkyl, C_{1-6} -acyl, hydroxy, oxo, t-butoxycarbonyl;

15 ONR^3R^4 , wherein R^3 and R^4 are each independently selected from hydrogen, C_{1-6} -alkyl or form together morpholinyl;

R^5O , wherein R^5 is hydrogen, optionally halogenated C_{1-6} -alkyl, aryl, heteroaryl, C_{1-6} -acyl, C_{1-6} -alkylsulfonyl, arylcarbonyl, heteroarylcarbonyl, 2-carbomethoxyphenyl; and pharmaceutically acceptable salts, solvates, hydrates, geometrical isomers, tautomers,

20 optical isomers, N-oxides and prodrug forms thereof.

2. The method according to claim 1, wherein

T is selected from 5-chloro-1,3-dimethyl-1H-pyrazol-4-yl; 4-chloro-2,3,1-benzoxadiazolyl; 5-(dimethylamino)-1-naphthyl; 1-methylimidazol-4-yl; 1-naphthyl; 2-naphthyl; (E)-2-phenylethenyl; 8-quinoliny;

25 thienyl substituted with one or more of (benzoylamino)methyl, bromo, chloro, 3-isoxazolyl, 2-(methylsulfanyl)-4-pyrimidinyl, 1-methyl-5-(trifluoromethyl)pyrazol-3-yl, phenylsulfonyl, pyridyl;

30 phenyl substituted with one or more of acetylamino, 3-acetylaminophenyl, 3-acetylphenyl, benzeneamino, 1,3-benzodioxol-5-yl, 2-benzofuryl, benzylamino, 3,5-bis(trifluoromethyl)phenyl, bromo, butoxy, carboxy, chloro, 4-carboxyphenyl, 3-chloro-2-cyanophenoxy, 4-chlorophenyl, 5-chloro-2-thienyl, cyano, 3,4-dichlorophenyl, ([4-

(2-ethoxy-2-oxoethyl)-1,3-thiazol-2-yl]amino}carbonyl), fluoro, 5-fluoro-2-methoxyphenyl, 2-furyl, hydrogen, iodo, isopropyl, methanesulfonyl, methoxy, methyl, 4-methyl-1-piperazinyl, 4-methyl-1-piperidinyl, 4-methylsulfanylphenyl, 5-methyl-2-thienyl, 4-morpholinyl, nitro, 3-nitrophenyl, phenoxy, phenyl, n-propyl, 4-pyridyl, 3-pyridylmethylamino, 1-pyrrolidinyl, 2-thienyl, 3-thienyl, 2-thienylmethylamino, trifluoromethoxy, 4-trifluoromethoxyphenyl, and trifluoromethyl;

R¹ is hydrogen or methyl;

10 X is CH₂ or CO;

Y is CH₂, CO or a single bond;

B is hydrogen or methyl;

15

R² is selected from n-propyl, azido, bromo, chloro, 2-pyridinylsulfanyl, 3-oxo-4-morpholinolylmethylene, ethoxycarbonyl, 5-methyl-1,3,4-oxadiazol-2-yl;

NR³R⁴, wherein R³ and R⁴ are each independently selected from acetyl, 1,3-benzodioxol-5-ylmethyl, benzyl, 3-chloro-2-methylphenylsulfonyl, cyclohexylmethyl, ethyl, 2-furylcarbonyl, 2-furylmethyl, hydrogen, 2-hydroxyethyl, 2-(1H-indol-3-yl)ethyl, isopropyl, methoxy, 2-methoxyethyl, methyl, 4-(1-methylimidazolyl)sulfonyl, methylsulfonyl, phenyl, propyl, trifluoromethylsulfonyl; or

NR³R⁴ represent together 4-acetylpiperazinyl, 4-t-butoxycarbonylpiperazinyl, 2-(3,4-dihydro-2(1H)isoquinolyl), (2R,6S)-2,6-dimethylmorpholinyl, (2R)-2,4-dimethyl-1-piperazinyl, 2-hydroxy-3-oxomorpholinyl, imidazolyl, 2-methyl-3-oxomorpholinyl, 4-methyl-2-oxopiperazinyl, 4-methylpiperazinyl, morpholinyl, (1S,4S)-2-oxa-5-aza-bicyclo[2.2.1]hept-5-yl, 2-oxoimidazolyl, 3-oxomorpholinyl, 3-oxo-1,4-oxazepinyl, 2-oxooxazolyl, piperazinyl; piperidinyl; pyrrolidinyl; pyrrolidonyl, thiomorpholinyl; 1,1-dioxido-thiomorpholinyl;

30 OCONR³R⁴, wherein R³ and R⁴ are each independently selected from ethyl, hydrogen or form together morpholinyl;

R⁵O, wherein R⁵ is selected from acetyl, benzoyl, benzyl, ethyl, 2-fluoroethyl, 2-furylcarbonyl, hydrogen, isobutyryl, isopropyl, methyl, 2-carbomethoxyphenyl, methylsulfonyl, phenyl, propionyl, 3-pyridinyl, and 2,2,2-trifluoroethyl.

- 5 3. The method according to any one of claims 1 or 2, wherein the compound is selected from:

ethyl (2-{[(2,4-dichloro-5-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl 2-(2-{[(4-chlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
10 ethyl 2-(2-{[(4-chloro-2,5-dimethylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl 2-(2-{[(2,4-difluorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl 2-(2-(((4-methylphenyl)sulfonyl)amino)-1,3-thiazol-4-yl)acetate,
ethyl 2-(2-{[(2,5-dichloro-3-thienyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
15 ethyl (2-{[(2-chlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl 2-{2-[(1,1'-biphenyl)-4-ylsulfonyl]amino}-1,3-thiazol-4-yl} acetate,
ethyl 2-(2-{[(3-bromophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(4-nitrophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
20 ethyl (2-{[(4-methoxyphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(3-nitrophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(3-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(3-chlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{[(4-fluorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
25 ethyl (2-{[(3-fluorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl {2-[(phenylsulfonyl)amino]-1,3-thiazol-4-yl} acetate,
ethyl (2-{[(4-isopropylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl [2-({3-({4-(2-ethoxy-2-oxoethyl)-1,3-thiazol-2-yl]amino } carbonyl)phenyl]sulfonyl } amino)-1,3-thiazol-4-yl]acetate,
30 ethyl [2-({4-({4-(2-ethoxy-2-oxoethyl)-1,3-thiazol-2-yl]amino } carbonyl)phenyl]sulfonyl } amino)-1,3-thiazol-4-yl]acetate,
ethyl (2-{[(2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetate,
ethyl [2-({2-(trifluoromethyl)phenyl]sulfonyl } amino)-1,3-thiazol-4-yl]acetate,

- ethyl [2-({[3-(trifluoromethyl)phenyl]sulfonyl}amino)-1,3-thiazol-4-yl]acetate,
ethyl [2-({[4-(trifluoromethyl)phenyl]sulfonyl}amino)-1,3-thiazol-4-yl]acetate,
ethyl 2-(2- {[(4-bromophenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl (2- {[(2-nitrophenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
5 ethyl (2- {[(2,4-dichloro-6-methylphenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl (2- {[(2,4,6-trichlorophenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl (2- {[(2,4-dichlorophenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl (2- {[(5-fluoro-2-methylphenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl (2- {[(4-propylphenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
10 ethyl (2- {[(2-methoxy-4-methylphenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl (2- {[(3,5-dichlorophenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl [2-({[4-(3-chloro-2-cyanophenoxy)phenyl]sulfonyl}amino)-1,3-thiazol-4-yl]acetate,
ethyl (2- {[(3,4-dichlorophenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
15 ethyl (2- {[(4-butoxyphenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl (2- {[(4-chloro-2-methylphenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl [2-({[4-(acetylamino)phenyl]sulfonyl}amino)-1,3-thiazol-4-yl]acetate,
ethyl {2-[(8-quinoliny)sulfonyl]amino}-1,3-thiazol-4-yl} acetate,
ethyl (2- {[(3,4-dimethoxyphenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
20 ethyl (2- {[(4-iodophenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl (2- {[(3-chloro-4-methylphenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl [2-({[5-(dimethylamino)-1-naphthyl]sulfonyl}amino)-1,3-thiazol-4-yl]acetate,
ethyl (2- {[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
25 ethyl (2- {[(5-bromo-2-methoxyphenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl (2- {[(2,5-dimethoxyphenyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
ethyl {2-[(2-naphthyl)sulfonyl]amino}-1,3-thiazol-4-yl} acetate,
ethyl {2-[(mesityl)sulfonyl]amino}-1,3-thiazol-4-yl} acetate,
ethyl (2- {[(3-bromo-5-chloro-2-thienyl)sulfonyl]amino }-1,3-thiazol-4-yl)acetate,
30 ethyl {2-[({[5-[(benzoylamino)methyl]-2-thienyl} sulfonyl]amino }-1,3-thiazol-4-yl} acetate,
ethyl {2-[({[5-[1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl]-2-thienyl} sulfonyl]amino }-1,3-thiazol-4-yl} acetate,

- ethyl (2-{{(4-cyanophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl {2-[(5-[2-(methylsulfanyl)-4-pyrimidinyl]-2-thienyl)sulfonyl]amino}-1,3-thiazol-4-yl} acetate,
ethyl (2-{{(3-cyanophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
5 ethyl (2-{{(2,4,5-trichlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl [2-{{(E)-2-phenylethenyl}sulfonyl}amino]-1,3-thiazol-4-yl]acetate,
ethyl (2-{{(2,3,4-trichlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(4-bromo-2,5-difluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl]acetate,
ethyl [2-{{[4-(trifluoromethoxy)phenyl}sulfonyl}amino]-1,3-thiazol-4-yl]acetate,
10 ethyl (2-{{(2,3-dichlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(2-bromophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(4,5-dichloro-2-thienyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl [2-{{[4-(phenylsulfonyl)-2-thienyl}sulfonyl}amino]-1,3-thiazol-4-yl]acetate,
ethyl [2-{{[5-(phenylsulfonyl)-2-thienyl}sulfonyl}amino]-1,3-thiazol-4-yl]acetate,
15 ethyl (2-{{(2,6-dichlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(2-cyanophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{[4-(acetylamino)-3-chlorophenyl}sulfonyl}amino]-1,3-thiazol-4-yl]acetate,
ethyl (2-{{(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
20 ethyl (2-{{(3-methoxyphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(4-bromo-5-chloro-2-thienyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl 2-{2-[(1-naphthylsulfonyl)amino]-1,3-thiazol-4-yl} acetate,
ethyl (2-{{(2,5-dichlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
25 ethyl (2-{{(4-methanesulfonylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(2-methanesulfonylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(4-bromo-2-fluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(2-methyl-4-trifluoromethoxyphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
30 ethyl (2-{{(2,3,4-trifluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
ethyl (2-{{[4-chloro-2,3,1-benzoxadiazolyl)sulfonyl}amino]-1,3-thiazol-4-yl)acetate,
ethyl (2-{{(2,4,6-trifluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,

- ethyl (2-{{(5-carboxy-4-chloro-2-fluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- ethyl (2-{{(2-(5-chlorothieryl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- ethyl (2-{{(2-chloro-4-fluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- 5 ethyl (2-{{(2-(5-(3-isoxazolo)thienyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- ethyl (2-{{(4-bromo-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- ethyl (2-{{(4-phenoxyphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- ethyl (2-{{(4-chloro-2,6-dimethylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- ethyl (2-{{(2-methyl-4-trifluoromethoxyphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- 10 ethyl (2-{{(2,4-bis(trifluoromethyl)phenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- ethyl 2-{2-[[{(3-chloro-2-methylphenyl)sulfonyl}(methyl)amino]-1,3-thiazol-4-yl}acetate,
- 15 ethyl oxo(2-{{(4-propylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- ethyl (2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)(oxo)acetate,
- ethyl oxo(2-{{(2,4,6-trichlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- ethyl {2-[[{(1,1'-biphenyl)-4-ylsulfonyl}amino]-1,3-thiazol-4-yl}(oxo)acetate,
- 20 ethyl (2-{{(2,4-dichloro-6-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)(oxo)acetate,
- 2-(2-{{(4-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetic acid,
- 2-(2-{{(2,5-dichloro-3-thienyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetic acid,
- (2-{{(2-chlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetic acid,
- 25 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetic acid,
- isopropyl 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- phenyl 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- methyl (2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- 30 methyl {2-[[{(1,1'-biphenyl)-4-ylsulfonyl}amino]-5-methyl-1,3-thiazol-4-yl}acetate,
- methyl (2-{{(4-chlorophenyl)sulfonyl}amino}-5-methyl-1,3-thiazol-4-yl)acetate,

- methyl (2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-5-methyl-1,3-thiazol-4-yl)acetate,
- methyl [2-{{(4-(3-chloro-2-cyanophenoxy)phenyl)sulfonyl}amino}-5-methyl-1,3-thiazol-4-yl]acetate,
- 5 methyl (5-methyl-2-{{(4-propylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- methyl (5-methyl-2-{{(2,4,6-trichlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetate,
- methyl (2-{{(2,4-dichloro-6-methylphenyl)sulfonyl}amino}-5-methyl-1,3-thiazol-4-yl)acetate,
- 10 N-(2-methoxyethyl)-2-(2-{{(4-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetamide,
- 2-(2-{{(2,5-dichloro-3-thienyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-methylacetamide,
- N-(1,3-benzodioxol-5-ylmethyl)-2-{2-[(1-naphthylsulfonyl)amino]-1,3-thiazol-4-yl}acetamide,
- 15 N-(2-furylmethyl)-2-{2-[(1-naphthylsulfonyl)amino]-1,3-thiazol-4-yl}acetamide,
- 2-(2-{{(2,4-difluorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-ethylacetamide,
- N-isopropyl-2-{2-[(1-naphthylsulfonyl)amino]-1,3-thiazol-4-yl}acetamide,
- N-[2-(1H-indol-3-yl)ethyl]-2-{2-[(1-naphthylsulfonyl)amino]-1,3-thiazol-4-yl}acetamide,
- 20 N-(cyclohexylmethyl)-2-{2-[(phenylsulfonyl)amino]-1,3-thiazol-4-yl}acetamide,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-methylacetamide,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-ethylacetamide,
- 25 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-phenylacetamide,
- 2-(2-{{(4-chlorophenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-(2-furylmethyl)acetamide,
- 30 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetamide,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N,N-diethylacetamide,

- 2-{2-[(1,1'-biphenyl)-4-ylsulfonyl]amino}-1,3-thiazol-4-yl}-N,N-diethylacetamide,
N,N-diethyl-2-(2-{[(4-propylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetamide,
2-(2-{[(2,4-dichloro-6-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N,N-
5 diethylacetamide,
N,N-diethyl-2-(2-{[(2,4,6-trichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetamide,
2-{2-[(1,1'-biphenyl)-4-ylsulfonyl]amino}-1,3-thiazol-4-yl}-N,N-diisopropylacetamide,
10 N,N-diisopropyl-2-(2-{[(4-propylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetamide,
2-(2-{[(2,4-dichloro-6-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N,N-diisopropylacetamide,
N,N-diisopropyl-2-(2-{[(2,4,6-trichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetamide,
15 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N,N-diisopropylacetamide,
2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N,N-dipropylacetamide,
20 N-benzyl-2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N-ethylacetamide,
2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N,N-dimethylacetamide,
3-chloro-N-{4-[2-(3,4-dihydro-2(1H)-isoquinoliny)-2-oxoethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide,
25 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N-methyl-N-phenylacetamide,
2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N-isopropyl-N-methylacetamide,
30 2-{2-[(1,1'-biphenyl)-4-ylsulfonyl]amino}-1,3-thiazol-4-yl}-N-isopropyl-N-methylacetamide,
N-ethyl-N-methyl-2-(2-{[(2,4,6-trichlorophenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetamide,

- 2-(2-{{(2,4-dichloro-6-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-ethyl-N-methylacetamide,
- N-ethyl-N-methyl-2-(2-{{(4-propylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)acetamide,
- 5 2-{2-[[[1,1'-biphenyl]-4-ylsulfonyl]amino]-1,3-thiazol-4-yl}-N-ethyl-N-methylacetamide,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)-N-ethyl-N-methylacetamide,
- 3-chloro-2-methyl-N-{4-[2-oxo-2-(1-pyrrolidiny)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 10 3-chloro-2-methyl-N-{4-[2-oxo-2-(1-piperidiny)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- N-{4-[2-oxo-2-(1-piperidiny)ethyl]-1,3-thiazol-2-yl}[1,1'-biphenyl]-4-sulfonamide,
- 15 N-{4-[2-oxo-2-(1-piperidiny)ethyl]-1,3-thiazol-2-yl}-4-propylbenzenesulfonamide,
- 2,4-dichloro-6-methyl-N-{4-[2-oxo-2-(1-piperidiny)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 2,4,6-trichloro-N-{4-[2-oxo-2-(1-piperidiny)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 20 3-chloro-2-methyl-N-{4-[2-(4-morpholiny)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 2,4,6-trichloro-N-{4-[2-(4-morpholiny)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 25 2,4-dichloro-6-methyl-N-{4-[2-(4-morpholiny)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- N-{4-[2-(4-morpholiny)-2-oxoethyl]-1,3-thiazol-2-yl}[1,1'-biphenyl]-4-sulfonamide,
- N-{4-[2-(4-morpholiny)-2-oxoethyl]-1,3-thiazol-2-yl}-4-propylbenzenesulfonamide,
- 30 2,4-dichloro-N-{4-[2-(4-morpholiny)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,

- 4-chloro-2,6-dimethyl-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}-4-
phenoxybenzenesulfonamide,
5 2-methyl-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}-4-(trifluoromethoxy)benzenesulfonamide,
N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}-2,4-bis(trifluoromethyl)benzenesulfonamide,
4-bromo-2-methyl-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-
10 yl}benzenesulfonamide,
4-(2-furyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
4-(5-fluoro-2-methoxyphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
15 4-(5-methyl-2-thienyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
4-(3-acetylphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
4-(4-trifluoromethoxyphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-
20 yl}benzenesulfonamide,
4-(3,4-dichlorophenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
4-(3,4-methylenedioxyphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
25 4-(5-chloro-2-thienyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
4-(4-pyridyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
4-(3-acetylaminophenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
30 4-(3-thienyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,

- 4-(2-thienyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(4-carboxyphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 5 4-(4-methylsulfanylphenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(3,5-bis(trifluoromethyl)phenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(4-chlorophenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 10 4-(3-nitrophenyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(2-benzofuryl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 15 4-(1-pyrrolidino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(4-methyl-1-piperidino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(benzeneamino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 20 4-(benzylamino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(2-thienylmethylamino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 25 4-(4-morpholinyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(4-methyl-1-piperazinyl)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 4-(3-pyridylmethylamino)-N-{4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 30 2,4-dichloro-6-methyl-N-{5-methyl-4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,

- N-{5-methyl-4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}[1,1'-biphenyl]-4-sulfonamide,
- 2,4,6-trichloro-N-{5-methyl-4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 5 3-chloro-2-methyl-N-{5-methyl-4-[2-(4-morpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 3-chloro-N-(4-{2-[(2R,6S)-2,6-dimethylmorpholinyl]-2-oxoethyl}-1,3-thiazol-2-yl)-2-methylbenzenesulfonamide,
- 3-chloro-2-methyl-N-(4-{2-[(1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl]-2-oxoethyl}-1,3-thiazol-2-yl)benzenesulfonamide,
- 10 3-chloro-2-methyl-N-{4-[2-oxo-2-(4-thiomorpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- N-{4-[2-oxo-2-(4-thiomorpholinyl)ethyl]-1,3-thiazol-2-yl}[1,1'-biphenyl]-4-sulfonamide,
- 15 N-{4-[2-oxo-2-(4-thiomorpholinyl)ethyl]-1,3-thiazol-2-yl}-4-propylbenzenesulfonamide,
- 2,4-dichloro-6-methyl-N-{4-[2-oxo-2-(4-thiomorpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 2,4,6-trichloro-N-{4-[2-oxo-2-(4-thiomorpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 20 N-{4-[2-(1,1-dioxido-4-thiomorpholinyl)-2-oxoethyl]-1,3-thiazol-2-yl}-4-propylbenzenesulfonamide,
- tert-butyl 4-[(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetyl]-1-piperazinecarboxylate,
- 25 4-acetyl-(4-[(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetyl])-1-piperazine,
- 4-[(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)acetyl]-1-piperazine trifluoroacetate,
- 3-chloro-2-methyl-N-{4-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide hydrochloride,
- 30 2-methyl-N-{4-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-1,3-thiazol-2-yl}-4-(trifluoromethoxy)benzenesulfonamide,

- 2,4-dichloro-6-methyl-N-{4-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 2,4-dichloro-N-{4-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 5 3-chloro-N-(4-{2-[(2R)-2,4-dimethylpiperazinyl]-2-oxoethyl}-1,3-thiazol-2-yl)-2-methylbenzenesulfonamide,
- 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)-N-methoxy-N-methylacetamide,
- 3-chloro-2-methyl-N-[4-(2-oxopentyl)-1,3-thiazol-2-yl]benzenesulfonamide,
- 10 4-chloro-N-[4-(2-hydroxyethyl)-1,3-thiazol-2-yl]benzenesulfonamide,
- 3-chloro-N-[4-(2-hydroxyethyl)-1,3-thiazol-2-yl]-2-methylbenzenesulfonamide,
- 3-chloro-N-[4-(2-ethoxyethyl)-1,3-thiazol-2-yl]-2-methylbenzenesulfonamide,
- 3-chloro-N-[4-(2-isopropoxyethyl)-1,3-thiazol-2-yl]-2-methylbenzenesulfonamide,
- 15 N-{4-[2-(benzyloxy)ethyl]-1,3-thiazol-2-yl}-3-chloro-2-methylbenzenesulfonamide,
- 3-chloro-N-[4-(2-methoxyethyl)-1,3-thiazol-2-yl]-2-methylbenzenesulfonamide,
- 3-chloro-N-{4-[2-(2-fluoroethoxy)ethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide,
- 20 3-chloro-2-methyl-N-{4-[2-(2,2,2-trifluoroethoxy)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 3-chloro-2-methyl-N-{4-[2-(2-pyridinylsulfanyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 3-chloro-2-methyl-N-{4-[2-(3-pyridinyloxy)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 25 3-chloro-2-methyl-N-{4-[2-methylsalicylethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
- 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)ethyl methanesulfonate,
- 30 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)ethyl acetate,
- 2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)ethyl propionate,

- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)ethyl 2-methylpropanoate,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)ethyl 2-furoate,
- 5 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)ethyl benzoate,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)ethyl 4-morpholinecarboxylate,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)ethyl
- 10 diethylcarbamate,
- 2-(2-{{(3-chloro-2-methylphenyl)sulfonyl}amino}-1,3-thiazol-4-yl)ethyl ethylcarbamate,
- N-[4-(2-azidoethyl)-1,3-thiazol-2-yl]-3-chloro-2-methylbenzenesulfonamide,
- N-[4-(2-aminoethyl)-1,3-thiazol-2-yl]-3-chloro-2-methylbenzenesulfonamide
- 15 hydrochloride,
- 4-chloro-N-{4-[2-(diethylamino)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide hydrochloride,
- 3-chloro-N-{4-[2-(diethylamino)ethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide hydrochloride,
- 20 3-chloro-N-{4-[2-(1-imidazolyl)ethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide hydrochloride,
- 3-chloro-2-methyl-N-{4-[2-(4-methyl-1-piperazinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide dihydrochloride,
- 3-chloro-2-methyl-N-{4-[2-(4-morpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide hydrochloride,
- 25 3-chloro-2-methyl-N-{4-[2-(4-morpholinyl)methyl]-1,3-thiazol-2-yl}benzenesulfonamide hydrochloride,
- 2,4,6-trichloro-N-{4-[2-(4-morpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide hydrochloride,
- 2,4-dichloro-N-{4-[2-(4-morpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide
- 30 hydrochloride,
- 2,4-dichloro-6-methyl-N-{4-[2-(4-morpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide hydrochloride,

- N-{4-[2-(4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-4-propylbenzenesulfonamide
hydrochloride,
- 3-chloro-N-{4-[2-(ethylamino)ethyl]-1,3-thiazol-2-yl}-2-
methylbenzenesulfonamide,
- 5 3-chloro-N-(4-{2-[(2-hydroxyethyl)amino]ethyl}-1,3-thiazol-2-yl)-2-
methylbenzenesulfonamide,
- N-[2-(2-{[(3-chloro-2-methylphenyl)sulfonyl]amino}-1,3-thiazol-4-yl)ethyl]-N-
ethylacetamide,
- 3-chloro-2-methyl-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-
10 yl}benzenesulfonamide,
- 3-chloro-N-{4-[2-(2-hydroxy-3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-2-
methylbenzenesulfonamide,
- 2,4-dichloro-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-
yl}benzenesulfonamide,
- 15 2,4-dichloro-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-6-
methylbenzenesulfonamide,
- N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-2,4,6-
trichlorobenzenesulfonamide,
- 4,5-dichloro-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-2-
20 thienylsulfonamide,
- N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-4-
phenoxybenzenesulfonamide,
- 3-fluoro-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-
yl}benzenesulfonamide,
- 25 N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}-5-(2-pyridyl)-2-
thienylsulfonamide,
- 4-acetylamino-3-chloro-N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-
yl}benzenesulfonamide,
- N-{4-[(3-oxo-4-morpholinyl)methyl]-1,3-thiazol-2-yl}-3-chloro-2-
30 methylbenzenesulfonamide,
- N-{4-[3-(3-oxo-4-morpholinyl)propyl]-1,3-thiazol-2-yl}-3-chloro-2-
methylbenzenesulfonamide,

- N-{4-[2-(3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl},N-methyl-3-chloro-2-methylbenzenesulfonamide,
3-chloro-2-methyl-N-{4-[2-(2-methyl-3-oxo-4-morpholinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
5 N-{4-[2-(acetylamino)ethyl]-1,3-thiazol-2-yl}-3-chloro-2-methylbenzenesulfonamide,
3-chloro-2-methyl-N-{4-[2-(4-(3-oxo-1,4-oxazepinyl))ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
3-chloro-2-methyl-N-{4-[2-(1-pyrrolidonyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
10 3-chloro-2-methyl-N-{4-[2-(1-(2-oxoimidazoliny))ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
3-chloro-2-methyl-N-{4-[2-(1-(2-oxooxazoliny))ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
15 3-chloro-N-{4-[2-(N-(2-furylcarbonyl),N-2-hydroxyethylamino)ethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide, hydrochloride,
3-chloro-2-methyl-N-{4-[2-(4-methyl-2-oxopiperazinyl)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
3-chloro-2-methyl-N-{4-[2-(methylsulfonylamino)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
20 3-chloro-2-methyl-N-{4-[2-(N-methyl,N-methylsulfonamino)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
3-chloro-2-methyl-N-{4-[2-(trifluoromethylsulfonylamino)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
25 3-chloro-2-methyl-N-{4-[2-(N-methyl,N-trifluoromethylsulfonamino)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
3-chloro-2-methyl-N-{4-[2-(4-(1-methylimidazolyl)sulfonylamino)ethyl]-1,3-thiazol-2-yl}benzenesulfonamide,
3-chloro-N-{4-[2-(N-(3-chloro-2-methylphenylsulfonyl),N-methylamino)ethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide,
30 N-[4-(2-bromoethyl)-1,3-thiazol-2-yl]-3-chloro-2-methylbenzenesulfonamide,
3-chloro-N-[4-(2-chloroethyl)-1,3-thiazol-2-yl]-2-methylbenzenesulfonamide,

3-chloro-2-methyl-N-{4-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-1,3-thiazol-2-yl}benzenesulfonamide, and
3-chloro-N-{4-[2-(ethoxycarbonyl)ethyl]-1,3-thiazol-2-yl}-2-methylbenzenesulfonamide.

- 5
4. The method according to any one of claims 1 to 3 for the treatment or prophylaxis of a medical condition involving delayed or impaired wound healing.
5. The method according to claim 4 wherein the medical condition involving delayed or
10 impaired wound healing is diabetes.
6. The method according to claim 4 wherein the medical condition involving delayed or impaired wound healing is caused by treatment with glucocorticoids.
- 15 7. The method according to any one of claims 1 to 3 for the promotion of wound healing in chronic wounds, such as diabetic ulcers, venous ulcers or pressure ulcers.
8. Use of a compound as defined in any one of claims 1 to 3 in the manufacture of a medicament for promoting wound healing, said compound being an inhibitor of 11- β -
20 hydroxysteroid dehydrogenase type 1.
9. The use according to claim 8 in the manufacture of a medicament for the treatment of prophylaxis of a medical condition involving delayed or impaired wound healing.
- 25 10. The use according to claim 9 wherein the medical condition involving delayed or impaired wound healing is diabetes.
11. The use according to claim 9 wherein the medical condition involving delayed or impaired wound healing is caused by treatment with glucocorticoids.
- 30 12. The use according to claim 8 in the manufacture of a medicament for the promotion of wound healing in chronic wounds, such as diabetic ulcers, venous ulcers or pressure ulcers.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 2004/000996

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61K 31/426, A61P 17/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61K, A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-INTERNAL, WPI DATA, CHEM. ABS DATA, MEDLINE DATA, EMBASE DATA, BIOSIS DATA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Stozowska, W. et al, "Urinary silver and sulfathiazole levels in thermally injured guinea pigs during treatment with silver sulfathiazole cream", S.T.P. Pharma Sciences, 1995, Vol. 5, no. 6, page 452 - page 455 --	1-12
X	GB 1240545 A (RESEARCH CORPORATION), 28 July 1971 (28.07.1971) --	1-12
A	WO 9631492 A1 (TEXAS BIOTECHNOLOGY CORPORATION), 10 October 1996 (10.10.1996) --	1-12

☒ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

15 October 2004

Date of mailing of the international search report

19-10-2004

Name and mailing address of the ISA/
 Swedish Patent Office
 Box 5055, S-102 42 STOCKHOLM
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 2004/000996

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 9816520 A1 (AMERICAN CYANAMID COMPANY), 23 April 1998 (23.04.1998) --	1-12
A	WO 0190090 A1 (BIOVITRUM AB), 29 November 2001 (29.11.2001) -- -----	1-12

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2004/000996

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **1-7**
because they relate to subject matter not required to be searched by this Authority, namely:
see next sheet
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2004/000996

Claims 1-7 relate to methods of treatment of the human or animal body by surgery or by therapy/ diagnostic methods practised on the human or animal body/Rule 39.1.(iv). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compounds/compositions.

INTERNATIONAL SEARCH REPORT

Information on patent family members

03/09/2004

International application No.

PCT/SE 2004/000996

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INTERNATIONAL SEARCH REPORT

Information on patent family members

03/09/2004

International application No.

PCT/SE 2004/000996

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INTERNATIONAL SEARCH REPORT
Information on patent family members

03/09/2004

International application No.
PCT/SE 2004/000996

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INTERNATIONAL SEARCH REPORT

Information on patent family members

03/09/2004

International application No.

PCT/SE 2004/000996

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