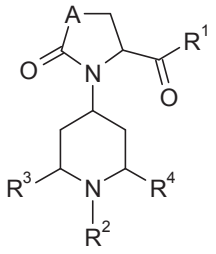
CLAIMS

1. Use of a compound of formula 1 or a salt thereof in the manufacture of a medicament for treating a skin disorder selected from pruritus, xerosis, and Bullous pemphigoid (BP), wherein the compound of formula 1 has the following formula:



1

wherein

A is CH_2, O or N-C_{1-6}-alkyl;

R^1 is selected from

- $NHR^{1.1}$, $NMeR^{1.1}$;
- $NHR^{1.2}$, $NMeR^{1.2}$;
- $NHCH_2$-$R^{1.3}$;
- NH-C_{3-6}-cycloalkyl, whereas optionally one carbon atom is replaced by a nitrogen atom, whereas the ring is optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, O-C_{1-6}-alkyl, $NHSO_2$-phenyl, NHCONH-phenyl, halogen, CN, SO_2-C_{1-6}-alkyl, COO-C_{1-6}-alkyl;
- a $C_{9\text{ or }10}$-bicyclic-ring, whereas one or two carbon atoms are replaced by nitrogen atoms and the ring system is bound via a nitrogen atom to the basic structure of formula **1** and whereas the ring system is optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, COO-C_{1-6}-alkyl, C_{1-6}-haloalkyl, O-C_{1-6}-alkyl, NO_2, halogen, CN, $NHSO_2$-C_{1-6}-alkyl, methoxy-phenyl;
- a group selected from NHCH(pyridinyl)CH_2COO-C_{1-6}-alkyl, NHCH(CH_2O-C_{1-6}-alkyl)-benzoimidazolyl, optionally substituted with halogen or CN;

- piperidinyl or substituted piperidinyl;
- or 1-aminocyclopentyl, optionally substituted with methyl-oxadiazole;

$R^{1.1}$ is phenyl, optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{1-6}-haloalkyl, C_{1-6}-alkylene-OH, C_{2-6}-alkenylene-OH, C_{2-6}-alkynylene-OH, $CH_2CON(C_{1-6}\text{-alkyl})_2$, $CH_2NHCONH\text{-}C_{3-6}$-cycloalkyl, CN, CO-pyridinyl, $CONR^{1.1.1}R^{1.1.2}$, $COO\text{-}C_{1-6}$-alkyl, $N(SO_2\text{-}C_{1-6}\text{-alkyl})(CH_2CON(C_{1-4}\text{-alkyl})_2)$ $O\text{-}C_{1-6}$-alkyl, O-pyridinyl, $SO_2\text{-}C_{1-6}$-alkyl, $SO_2\text{-}C_{1-6}$-alkylen-OH, $SO_2\text{-}C_{3-6}$-cycloalkyl, SO_2-piperidinyl, $SO_2NH\text{-}C_{1-6}$-alkyl, $SO_2N(C_{1-6}\text{-alkyl})_2$, halogen, CN, CO-morpholinyl, CH_2-pyridinyl or a heterocyclic ring optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, NHC_{1-6}-alkyl and =O;

$R^{1.1.1}$ H, C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{1-6}-haloalkyl, $CH_2CON(C_{1-6}\text{-alkyl},)_2$, CH_2CO-azetindinyl, C_{1-6}-alkylen-C_{3-6}-cycloalkyl, CH_2-pyranyl, CH_2-tetrahydrofuranyl, CH_2-furanyl, C_{1-6}-alkylen-OH or thiadiazolyl, optionally substituted with C_{1-6}-alkyl;

$R^{1.1.2}$ H, C_{1-6}-alkyl, SO_2C_{1-6}-alkyl;

or $R^{1.1.1}$ and $R^{1.1.2}$ together ~~are forming~~form a four-, five- or six-membered ~~carbocyclic~~ ring~~, optionally~~ containing one N~~ or O~~, replacing a carbon atom of the ring, optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, C_{1-4}-alkylene-OH, OH, =O~~, or $R^{1.1.1}$ and $R^{1.1.2}$ together with a nitrogen atom form a heterocyclic ring~~;

or

$R^{1.1}$ is phenyl, wherein two adjacent residues are together forming a five- or six-membered carbocyclic aromatic or non-aromatic ring, optionally containing independently from each other one or two N, S, or SO_2, replacing a carbon atom of the ring, wherein the ring is optionally substituted with C_{1-4}-alkyl or =O;

$R^{1.2}$ is selected from

- heteroaryl, optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{3-6}-cycloalkyl, CH_2COO-C_{1-6}-alkyl, $CONR^{1.2.1}R^{1.2.2}$, $COR^{1.2.3}$, COO-C_{1-6}-alkyl, $CONH_2$, O-C_{1-6}-alkyl, halogen, CN, $SO_2N(C_{1-6}$-alkyl$)_2$ or heteroaryl optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl;
- heteroaryl, optionally substituted with a five- or six-membered carbocyclic non-aromatic ring containing independently from each other two N, O, S, or SO_2, replacing a carbon atom of the ring;
- an aromatic or non-aromatic $C_{9\text{ or }10}$-bicyclic-ring, whereas one or two carbon atoms are replaced by N, O or S each optionally substituted with one or two residues selected from the group consisting of $N(C_{1-6}$-alkyl$)_2$, CONH-C_{1-6}-alkyl, =O;
- a heterocyclic non-aromatic ring, optionally substituted with pyridinyl;
- 4,5-dihydro-naphtho[2,1-d]thiazole, optionally substituted with NHCO-C_{1-6}-alkyl,

$R^{1.2.1}$ H, C_{1-6}-alkyl, C_{1-6}-alkylene-C_{3-6}-cycloalkyl, C_{1-4}-alkylene-phenyl, C_{1-4}-alkylene-furanyl, C_{3-6}-cycloalkyl, C_{1-4}-alkylene-O-C_{1-4}-alkyl, C_{1-6}-haloalkyl or a five- or six-membered carbocyclic non-aromatic ring, optionally containing independently from each other one or two N, O, S, or SO_2, replacing a carbon atom of the ring, optionally substituted with 4-cyclopropylmethyl-piperazinyl;

$R^{1.2.2}$ H, C_{1-6}-alkyl;

$R^{1.2.3}$ a five- or six-membered carbocyclic non-aromatic ring, optionally containing independently from each other one or two N, O, S, or SO_2, replacing a carbon atom of the ring;

$R^{1.3}$ is selected from phenyl, heteroaryl or indolyl, each optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, C_{3-6}-cycloalkyl, O-C_{1-6}-alkyl, O-C_{1-6}-haloalkyl, phenyl, heteroaryl;

R^2 is selected from the group consisting of C_{1-6}-alkylene-phenyl, C_{1-6}-alkylene-naphthyl, and C_{1-6}-alkylene-heteroaryl; each optionally substituted with one, two or three residues selected from the group consisting of C_{1-6}-alkyl, C_{1-6}-haloalkyl, O-C_{1-6}-alkyl, O-C_{1-6}-haloalkyl, halogen;

R^3 is H, C_{1-6}-alkyl;

R^4 is H, C_{1-6}-alkyl;

or **R^3** and **R^4** together are forming a CH_2-CH_2 group.

2. The use of the compound or a salt thereof of claim 1, wherein in the compound of formula 1,

A is CH_2, O or N-C_{1-4}-alkyl;

R^1 is selected from

- $NHR^{1.1}$, $NMeR^{1.1}$;
- $NHR^{1.2}$, $NMeR^{1.2}$;
- $NHCH_2$-$R^{1.3}$;
- NH-C_{3-6}-cycloalkyl, whereas optionally one carbon atom is replaced by a nitrogen atom, whereas the ring is optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, O-C_{1-6}-alkyl, $NHSO_2$-phenyl, NHCONH-phenyl, halogen, CN, SO_2-C_{1-6}-alkyl, COO-C_{1-6}-alkyl;
- a $C_{9\text{ or }10}$-bicyclic-ring, whereas one or two carbon atoms are replaced by nitrogen atoms and the ring system is bound via a nitrogen atom to the basic structure of formula **1** and whereas the ring system is optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, COO-C_{1-6}-alkyl, C_{1-6}-haloalkyl, O-C_{1-6}-alkyl, NO_2, halogen, CN, $NHSO_2$-C_{1-6}-alkyl, m-methoxyphenyl;
- a group selected from NHCH(pyridinyl)CH_2COO-C_{1-6}-alkyl, NHCH(CH_2O-C_{1-6}-alkyl)-benzoimidazolyl, optionally substituted with Cl;
- piperidinyl or substituted piperidinyl;

- or 1-aminocyclopentyl, optionally substituted with methyl-oxadiazolyl;

$R^{1.1}$ is phenyl, optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, C_{1-6}-haloalkyl, $CH_2CON(C_{1-6}$-alkyl$)_2$, $CH_2NHCONH$-C_{3-6}-cycloalkyl, CN, $CONR^{1.1.1}R^{1.1.2}$, COO-C_{1-6}-alkyl, O-C_{1-6}-alkyl, SO_2-C_{1-6}-alkyl, SO_2-C_{1-6}-alkylen-OH, SO_2-C_{3-6}-cycloalkyl, SO_2-piperidinyl, SO_2NH-C_{1-6}-alkyl, $SO_2N(C_{1-6}$-alkyl$)_2$, halogen, CN, CO-morpholinyl, CH_2-pyridinyl or a heterocyclic ring optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, NHC_{1-6}-alkyl,, =O;

$R^{1.1.1}$ H, C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{1-6}-haloalkyl, $CH_2CON(C_{1-6}$-alkyl,$)_2$, CH_2CO-azetindinyl, C_{1-6}-alkylen-C_{3-6}-cycloalkyl, CH_2-pyranyl, CH_2-tetrahydrofuranyl, CH_2-furanyl, C_{1-6}-alkylen-OH or thiadiazolyl, optionally substituted with C_{1-6}-alkyl;

$R^{1.1.2}$ H, C_{1-6}-alkyl, SO_2C_{1-6}-alkyl;

or $R^{1.1.1}$ and $R^{1.1.2}$ together ~~are forming~~form a four-, five- or six-membered ~~carbocyclic~~ ring~~, optionally~~ containing one ~~O~~N, replacing a carbon atom of the ring, optionally substituted with one or two residues selected from the group consisting of CH_2OH;

$R^{1.2}$ is selected from

- heteroaryl, optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, C_{3-6}-cycloalkyl, CH_2COO-C_{1-6}-alkyl, $CONR^{1.2.1}R^{1.2.2}$, COO-C_{1-6}-alkyl, $CONH_2$, O-C_{1-6}-alkyl, halogen, CN, CO-pyrrolidinyl, CO-morpholinyl or heteroaryl optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl;
- benzothiazolyl, indazolyl, dihydro-indolyl, indanyl, tetrahydro-quinolinyl, each optionally substituted with one or two residues selected from the group consisting of $N(C_{1-6}$-alkyl$)_2$, $CONH$-C_{1-6}-alkyl, =O;
- piperidinyl, optionally substituted with pyridinyl;

- 4,5-dihydro-naphtho[2,1-d]thiazole, optionally substituted with NHCO-C_{1-6}-alkyl,

$R^{1.2.1}$ H, C_{1-6}-alkyl;

$R^{1.2.2}$ H, C_{1-6}-alkyl;

$R^{1.3}$ is selected from phenyl, pyrazolyl, isoxazolyl, pyrimidinyl, indolyl or oxadiazolyl, each optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, C_{3-6}-cycloalkyl, O-C_{1-6}-alkyl, O-C_{1-6}-haloalkyl;

R^2 is selected from CH_2-phenyl or CH_2-naphthyl, both optionally substituted with one or two residues selected from the group consisting of C_{1-6}-alkyl, C_{1-6}-haloalkyl, O-C_{1-6}-alkyl, O-C_{1-6}-haloalkyl, halogen; or CH_2-thiophenyl, optionally substituted with one or two residues selected from the group consisting of halogen;

R^3 is H, C_{1-4}-alkyl;

R^4 is H, C_{1-4}-alkyl;

or **R^3** and **R^4** together are forming a CH_2-CH_2 group.

3. The use of the compound or a salt thereof of claim 1, wherein in the compound of formula 1:

A is CH_2, O or NMe;

R^1 is selected from

- $NHR^{1.1}$, $NMeR^{1.1}$;
- $NHR^{1.2}$, $NMeR^{1.2}$;
- $NHCH_2$-$R^{1.3}$;
- NH-cyclohexyl, optionally substituted with one or two residues selected from the group consisting of C_{1-4}-alkyl, $NHSO_2$-phenyl, NHCONH-phenyl, halogen;
- NH-pyrrolidinyl, optionally substituted with one or two residues selected from the group consisting of SO_2-C_{1-4}-alkyl, COO-C_{1-4}-alkyl;

- piperidinyl, optionally substituted with one or two residues selected from the group consisting of $NHSO_2$-C_{1-4}-alkyl, m-methoxyphenyl;
- dihydro-indolyl, dihydro-isoindolyl, tetrahydro-quinolinyl or tetrahydro-isoquinolinyl, optionally substituted with one or two residues selected from the group consisting of C_{1-4}-alkyl, COO-C_{1-4}-alkyl, C_{1-4}-haloalkyl, O-C_{1-4}-alkyl, NO_2, halogen;
- a group selected from $NHCH(pyridinyl)CH_2COO$-C_{1-4}-alkyl, $NHCH(CH_2O$-C_{1-4}-alkyl)-benzoimidazolyl, optionally substituted with Cl;
- or 1-aminocyclopentyl, optionally substituted with methyl-oxadiazolyl;

$R^{1.1}$ is phenyl, optionally substituted with one or two residues selected from the group consisting of C_{1-4}-alkyl, C_{1-4}-haloalkyl, $CH_2CON(C_{1-4}$-alkyl$)_2$, $CH_2NHCONH$-C_{3-6}-cycloalkyl, CN, $CONR^{1.1.1}R^{1.1.2}$, COO-C_{1-4}-alkyl, O-C_{1-4}-alkyl, SO_2-C_{1-4}-alkyl, SO_2-C_{1-4}-alkylen-OH, SO_2-C_{3-6}-cycloalkyl, SO_2-piperidinyl, SO_2NH-C_{1-4}-alkyl, $SO_2N(C_{1-4}$-alkyl$)_2$, halogen, CO-morpholinyl, CH_2-pyridinyl, or imidazolidinyl, piperidinyl, oxazinanyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, oxadiazolyl, thiazolyl, pyridinyl, pyrimidinyl, each optionally substituted with one or two residues selected from the group consisting of C_{1-4}-alkyl, NHC_{1-4}-alkyl,, =O;

$R^{1.1.1}$ H, C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{1-4}-haloalkyl, $CH_2CON(C_{1-4}$-alkyl,$)_2$, CH_2CO-azetindinyl, C_{1-4}-alkylen-C_{3-6}-cycloalkyl, CH_2-pyranyl, CH_2-tetrahydrofuranyl, CH_2-furanyl, C_{1-4}-alkylen-OH or thiadiazolyl, optionally substituted with C_{1-4}-alkyl;

$R^{1.1.2}$ H, C_{1-4}-alkyl, SO_2C_{1-4}-alkyl;

or $R^{1.1.1}$ and $R^{1.1.2}$ together ~~are forming~~form a four-, five- or six-membered ~~carbocyclic~~ ring~~, optionally~~ containing one ~~O~~N, replacing a carbon atom of the ring, optionally substituted with one or two residues selected from the group consisting of CH_2OH;

$R^{1.2}$ is selected from

- pyridinyl, pyridazinyl, pyrrolyl, pyrazolyl, isoxazolyl, thiazolyl, thiadiazolyl, optionally substituted with one or two residues selected from the group consisting of C_{1-4}-alkyl, C_{3-6}-cycloalkyl, CH_2COO-C_{1-4}-alkyl, $CONR^{1.2.1}R^{1.2.2}$, COO-C_{1-4}-alkyl, $CONH_2$, O-C_{1-4}-alkyl, halogen, CO-pyrrolidinyl, CO-morpholinyl or pyrazolyl, triazolyl, tetrazolyl, isoxazolyl, oxadiazolyl, each optionally substituted with one or two residues selected from the group consisting of C_{1-4}-alkyl;
- benzothiazolyl, indazolyl, dihydro-indolyl, indanyl, tetrahydro-quinolinyl, each optionally substituted with one or two residues selected from the group consisting of $N(C_{1-4}\text{-alkyl})_2$, $CONH$-C_{1-4}-alkyl, =O;
- piperidinyl, optionally substituted with pyridinyl;
- 4,5-dihydro-naphtho[2,1-d]thiazole, optionally substituted with $NHCO$-C_{1-4}-alkyl,

$R^{1.2.1}$ H, C_{1-4}-alkyl;

$R^{1.2.2}$ H, C_{1-4}-alkyl;

$R^{1.3}$ is selected from phenyl, pyrazolyl, isoxazolyl, pyrimidinyl, indolyl or oxadiazolyl, each optionally substituted with one or two residues selected from the group consisting of C_{1-4}-alkyl, C_{3-6}-cycloalkyl, O-C_{1-4}-alkyl, O-C_{1-4}-haloalkyl;

R^2 is selected from CH_2-phenyl or CH_2-naphthyl, both optionally substituted with one or two residues selected from the group consisting of C_{1-4}-alkyl, C_{1-4}-haloalkyl, O-C_{1-4}-haloalkyl, halogen; or CH_2-thiophenyl, optionally substituted with one or two residues selected from the group consisting of halogen;

R^3 is H;

R^4 is H;

or **R^3** and **R^4** together are forming a CH_2-CH_2 group.

4. The use of the compound or a salt thereof of claim 1, wherein in the compound of formula 1:

A is CH_2, O or NMe;

R^1 is selected from

- $NHR^{1.1}$, $NMeR^{1.1}$;
- $NHR^{1.2}$, $NMeR^{1.2}$;
- $NHCH_2$-$R^{1.3}$;
- NH-piperidinyl, optionally substituted with pyridinyl;
- NH-cyclohexyl, optionally substituted with one or two residues selected from the group consisting of t-Bu, $NHSO_2$-phenyl, NHCONH-phenyl, F;
- NH-pyrrolidinyl, optionally substituted with one or two residues selected from the group consisting of SO_2Me, COO-t-Bu;
- piperidinyl, optionally substituted with one or two residues selected from the group consisting of $NHSO_2$-n-Bu, m-methoxyphenyl;
- dihydro-indolyl, dihydro-isoindolyl, tetrahydro-quinolinyl or tetrahydro-isoquinolinyl, optionally substituted with one or two residues selected from the group consisting of Me, COOMe, CF_3, OMe, NO_2, F, Br;
- a group selected from NHCH(pyridinyl)CH_2COOMe, NHCH(CH_2OMe)-benzoimidazolyl, optionally substituted with Cl;
- or 1-aminocyclopentyl, optionally substituted with methyl-oxadiazolyl;

$R^{1.1}$ is phenyl, optionally substituted with one or two residues selected from the group consisting of Me, Et, t-Bu, CF_3, CH_2CONMe_2, CH_2NHCONH-cyclohexyl, CN, $CONR^{1.1.1}R^{1.1.2}$, COOMe, COOEt, OMe, SO_2Me, $SO_2CH_2CH_2OH$, SO_2Et, SO_2-cyclopropyl, SO_2-piperidinyl, SO_2NHEt, SO_2NMeEt, F, Cl, CO-morpholinyl, CH_2-pyridinyl, or imidazolidinyl, piperidinyl, oxazinanyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, oxadiazolyl, thiazolyl, pyridinyl, pyrimidinyl, each optionally

substituted with one or two residues selected from the group consisting of Me, NHMe, =O;

$R^{1.1.1}$ H, Me, Et, t-Bu, i-Pr, cyclopropyl, CH_2-i-Pr, CH_2-t-Bu, $CH(CH_3)CH_2CH_3$, CH_2CHF_2, CH_2CONMe_2, CH_2CO-azetindinyl, CH_2-cyclopropyl, CH_2-cyclobutyl, CH_2-pyranyl, CH_2-tetrahydro-furanyl, CH_2-furanyl, CH_2CH_2OH or thiadiazolyl, optionally substituted with Me;

$R^{1.1.2}$ H, Me, Et, SO_2Me, SO_2Et

or $R^{1.1.1}$ and $R^{1.1.2}$ together ~~are forming~~**form** a four-, five- or six-membered ~~carbocyclic~~ ring~~, optionally~~ containing one ~~O~~**N**, replacing a carbon atom of the ring, optionally substituted with one or two residues selected from the group consisting of CH_2OH;

$R^{1.2}$ is selected from

- pyridinyl, pyrrolyl, pyrazolyl, isoxazolyl, thiazolyl, thiadiazolyl, optionally substituted with one or two residues selected from the group consisting of Me, Et, Pr, Bu, cyclopropyl, CH_2COOEt, $CONR^{1.2.1}R^{1.2.2}$, COOMe, COOEt, $CONH_2$, OMe, Cl, Br CO-pyrrolidinyl, CO-morpholinyl or pyrazolyl, triazolyl, tetrazolyl, isoxazolyl, oxadiazolyl, each optionally substituted Me;
- benzothiazolyl, indazolyl, dihydro-indolyl, indanyl, tetrahydro-quinolinyl, each optionally substituted with one or two residues selected from the group consisting of NMe_2, CONHMe, =O;
- 4,5-dihydro-naphtho[2,1-d]thiazole, optionally substituted with NHCOMe,

$R^{1.2.1}$ H, Me;

$R^{1.2.2}$ H, Me;

$R^{1.3}$ is selected from phenyl, pyrazolyl, isoxazolyl, pyrimidinyl, indolyl or oxadiazolyl, each optionally substituted with one or two residues selected from the group consisting of Me, Et, Pr, cyclopentyl, OMe, $OCHF_2$;

R^2 is selected from CH_2-phenyl or CH_2-naphthyl, both optionally substituted with one or two residues selected from the group consisting of CH_3, CF_3, OCF_3, F, Cl, Br, Et; or CH_2-thiophenyl, optionally substituted with one or two residues selected from the group consisting of Cl, Br;

R^3 is H;

R^4 is H;

or **R^3** and **R^4** together are forming a CH_2-CH_2 group.

5. The use of the compound or a salt thereof of claim 1, wherein in the compound of formula 1:

A is CH_2, O or NMe;

R^1 is selected from

- $NHR^{1.1}$
- $NHR^{1.2}$,

$R^{1.1}$ is phenyl, optionally substituted with one or two residues selected from the group consisting of Me, Et, Bu, CF_3, CH_2CONMe_2, $CH_2NHCONH$-cyclohexyl, CN, $CONR^{1.1.1}R^{1.1.2}$, COOMe, COOEt, OMe, SO_2Me, $SO_2CH_2CH_2OH$, SO_2Et, SO_2-cyclopropyl, SO_2-piperidinyl, SO_2NHEt, SO_2NMeEt, F, Cl, CO-morpholinyl, CH_2-pyridinyl, or imidazolidinyl, piperidinyl, oxazinanyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, oxadiazolyl, thiazolyl, pyridinyl, pyrimidinyl, each optionally substituted with one or two residues selected from the group consisting of Me, NHMe, =O;

$R^{1.1.1}$ H, Me, Et, t-Bu, i-Pr, cyclopropyl, CH_2-i-Pr, CH_2-t-Bu, $CH(CH_3)CH_2CH_3$, CH_2CHF_2, CH_2CONMe_2, CH_2CO-azetindinyl, CH_2-cyclopropyl, CH_2-cyclobutyl, CH_2-pyranyl, CH_2-tetrahydro-

furanyl, CH_2-furanyl, CH_2CH_2OH or thiadiazolyl, optionally substituted with Me;

$R^{1.1.2}$ H, Me, Et, SO_2Me, SO_2Et

or $R^{1.1.1}$ and $R^{1.1.2}$ together are forming a four-, five- or six-membered ~~carbocyclic~~ ring~~, optionally~~ containing one O, replacing a carbon atom of the ring, optionally substituted with one or two residues selected from the group consisting of CH_2OH;

$R^{1.2}$ is selected from

- pyridinyl, pyrrolyl, pyrazolyl, isoxazolyl, thiazolyl, thiadiazolyl, optionally substituted with one or two residues selected from the group consisting of Me, Et, Pr, Bu, cyclopropyl, CH_2COOEt, $CONR^{1.2.1}R^{1.2.2}$, COOMe, COOEt, $CONH_2$, OMe, Cl, Br CO-pyrrolidinyl, CO-morpholinyl or pyrazolyl, triazolyl, tetrazolyl, isoxazolyl, oxadiazolyl, each optionally substituted Me;
- benzothiazolyl, indazolyl, dihydro-indolyl, indanyl, tetrahydro-quinolinyl, each optionally substituted with one or two residues selected from the group consisting of NMe_2, CONHMe, =O;
- 4,5-dihydro-naphtho[2,1-d]thiazole, optionally substituted with NHCOMe,

$R^{1.2.1}$ H, Me;

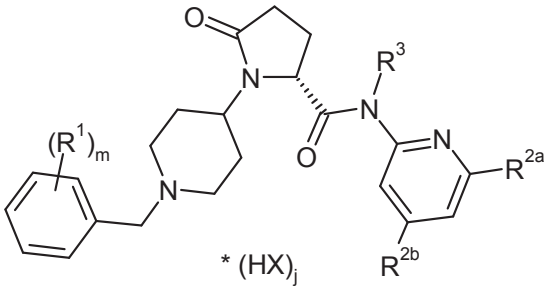
$R^{1.2.2}$ H, Me;

R^2 is selected from CH_2-phenyl or CH_2-naphthyl, both optionally substituted with one or two residues selected from the group consisting of CH_3, CF_3, OCF_3, F, Cl, Br, Et;

R^3 is H;

R^4 is H.

6. The use of the compound or a salt thereof of claim 1, wherein the compound is a co-crystal of formula



wherein

R^1 is C_{1-6}-alkyl, C_{1-6}-haloalkyl, O-C_{1-6}-haloalkyl, halogen;

m is 1, 2 or 3;

R^{2a} and R^{2b} are each independently selected from H, C_{1-6}-alkyl, C_{1-6}-alkenyl, C_{1-6}-alkynyl, C_{3-6}-cycloalkyl, COO-C_{1-6}-alkyl, O-C_{1-6}-alkyl, $CONR^{2b.1}R^{2b.2}$, halogen;

$R^{2b.1}$ is H, C_{1-6}-alkyl, C_{0-4}-alkyl-C_{3-6}-cycloalkyl, C_{1-6}-haloalkyl;

$R^{2b.2}$ is H, C_{1-6}-alkyl;

or $R^{2b.1}$ and $R^{2b.2}$ are together a C_{3-6}-alkylene group forming with the nitrogen atom a heterocyclic ring, wherein optionally one carbon atom or the ring is replaced by an oxygen atom

R^3 is H, C_{1-6}-alkyl;

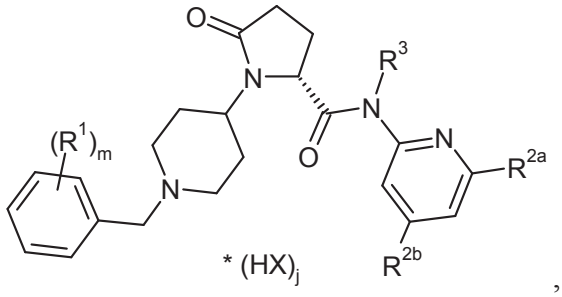
X is an anion selected from the group consisting of chloride, bromide, iodide, sulphate, phosphate, methanesulphonate, nitrate, maleate, acetate, benzoate, citrate, salicylate, fumarate, tartrate, dibenzoyltartrate, oxalate, succinate, benzoate and p-toluenesulphonate;

j is 0, 0.5, 1, 1.5 or 2;

with a co-crystal former selected from the group consisting of orotic acid, hippuric acid, L-pyroglutamic acid, D-pyroglutamic acid, nicotinic acid, L-(+)-ascorbic acid, saccharin, piperazine, 3-hydroxy-2-naphtoic acid, mucic (galactaric)

acid, pamoic (embonic) acid, stearic acid, cholic acid, deoxycholic acid, nicotinamide, isonicotinamide, succinamide, uracil, L-lysine, L-proline, D-valine, L-arginine, glycine.

7. The use of the compound or a salt thereof of claim 1, wherein the compound is a co-crystal of formula



,

wherein:

R^1 is C_{1-6}-alkyl, C_{1-6}-haloalkyl, O-C_{1-6}-haloalkyl, halogen;

m is 1, 2 or 3;

R^{2a} is H, C_{1-6}-alkyl, C_{1-6}-alkenyl, C_{1-6}-alkynyl, C_{3-6}-cycloalkyl, O-C_{1-6}-alkyl, $CONR^{2a.1}R^{2a.2}$;

$R^{2a.1}$ is H, C_{1-6}-alkyl, C_{1-6}-haloalkyl;

$R^{2a.2}$ is H, C_{1-6}-alkyl;

R^{2b} is H, C_{1-6}-alkyl, C_{1-6}-alkenyl, C_{1-6}-alkynyl, C_{3-6}-cycloalkyl, COO-C_{1-6}-alkyl, O-C_{1-6}-alkyl, $CONR^{2b.1}R^{2b.2}$, halogen;

$R^{2b.1}$ is H, C_{1-6}-alkyl, C_{0-4}-alkyl-C_{3-6}-cycloalkyl, C_{1-6}-haloalkyl;

$R^{2b.2}$ is H, C_{1-6}-alkyl;

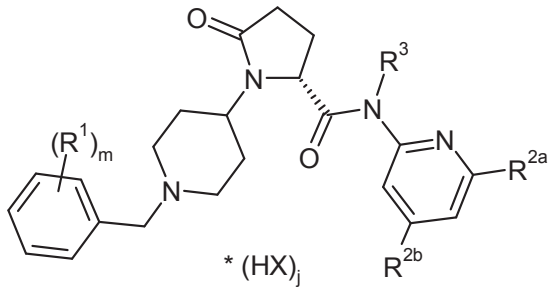
or $R^{2b.1}$ and $R^{2b.2}$ are together a C_{3-6}-alkylene group forming with the nitrogen atom a heterocyclic ring, wherein optionally one carbon atom or the ring is replaced by an oxygen atom**;**

R^3 is H, C_{1-6}-alkyl;

X is an anion selected from the group consisting of chloride, bromide, iodide, sulphate, phosphate, methanesulphonate, nitrate, maleate, acetate, benzoate, citrate, salicylate, fumarate, tartrate, dibenzoyltartrate, oxalate, succinate, benzoate and p-toluenesulphonate;

j is 0, 0.5, 1, 1.5 or 2.

8. The use of the compound or a salt thereof of claim 1, wherein the compound is a co-crystal of formula



R^1 is C_{1-6}-alkyl, C_{1-6}-haloalkyl, O-C_{1-6}-haloalkyl, halogen;

m is 1 or 2;

R^{2a} is H, C_{1-4}-alkyl;

R^{2b} is H, $CONR^{2b.1}R^{2b.2}$;

$R^{2b.1}$ is C_{1-4}-alkyl, C_{0-4}-alkyl-C_{3-6}-cycloalkyl, C_{1-4}-haloalkyl;

$R^{2b.2}$ is H, C_{1-4}-alkyl;

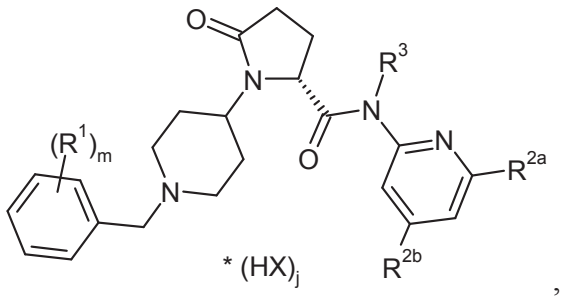
or $R^{2b.1}$ and $R^{2b.2}$ are together a C_{3-6}-alkylene group forming with the nitrogen atom a heterocyclic ring, wherein optionally one carbon atom or the ring is replaced by an oxygen atom

R^3 is H, C_{1-6}-alkyl;

X is an anion selected from the group consisting of chloride or dibenzoyltartrate

j is 1 or 2.

9. The use of the compound or a salt thereof of claim 1, wherein the compound is a co-crystal of formula



,

wherein:

R^1 is C_{1-6}-alkyl, C_{1-6}-haloalkyl, O-C_{1-6}-haloalkyl, halogen;

m is 1, 2 or 3;

R^3 is H, C_{1-6}-alkyl;

X is an anion selected from the group consisting of chloride, bromide, iodide, sulphate, phosphate, methanesulphonate, nitrate, maleate, acetate, benzoate, citrate, salicylate, fumarate, tartrate, dibenzoyltartrate, oxalate, succinate, benzoate and p-toluenesulphonate;

j is 0, 0.5, 1, 1.5 or 2;

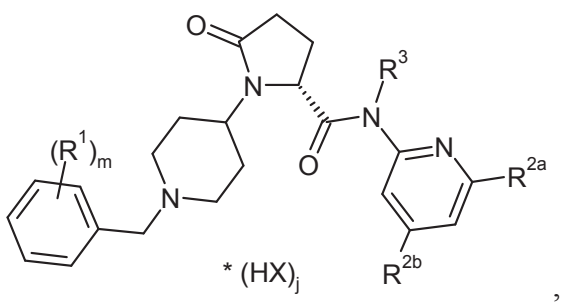
R^{2a} is H, C_{1-4}-alkyl;

R^{2b} is H, $CONR^{2b.1}R^{2b.2}$;

$R^{2b.1}$ is C_{1-4}-alkyl;

$R^{2b.2}$ is C_{1-4}-alkyl.

10. The use of the compound or a salt thereof of claim 1, wherein the compound is a co-crystal of formula



,

wherein:

R^1 is C_{1-6}-alkyl, C_{1-6}-haloalkyl, O-C_{1-6}-haloalkyl, halogen;

m is 1, 2 or 3;

R^3 is H, C_{1-6}-alkyl;

X is an anion selected from the group consisting of chloride, bromide, iodide, sulphate, phosphate, methanesulphonate, nitrate, maleate, acetate, benzoate, citrate, salicylate, fumarate, tartrate, dibenzoyltartrate, oxalate, succinate, benzoate and p-toluenesulphonate;

j is 0, 0.5, 1, 1.5 or 2;

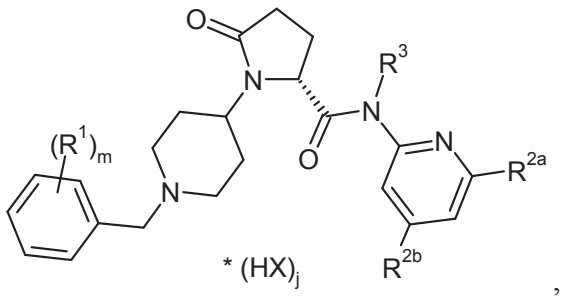
R^{2a} is H, C_{1-4}-alkyl;

R^{2b} is H, $CONR^{2b.1}R^{2b.2}$;

$R^{2b.1}$ is C_{0-4}-alkyl-C_{3-6}-cycloalkyl;

$R^{2b.2}$ is H, C_{1-4}-alkyl.

11. The use of the compound or a salt thereof of claim 1, wherein the compound is a co-crystal of formula



,

wherein:

R^1 is C_{1-6}-alkyl, C_{1-6}-haloalkyl, O-C_{1-6}-haloalkyl, halogen;

m is 1, 2 or 3;

R^3 is H, C_{1-6}-alkyl;

X is an anion selected from the group consisting of chloride, bromide, iodide, sulphate, phosphate, methanesulphonate, nitrate, maleate, acetate, benzoate,

citrate, salicylate, fumarate, tartrate, dibenzoyltartrate, oxalate, succinate, benzoate and p-toluenesulphonate;

j is 0, 0.5, 1, 1.5 or 2;

R^{2a} is H, C_{1-4}-alkyl;

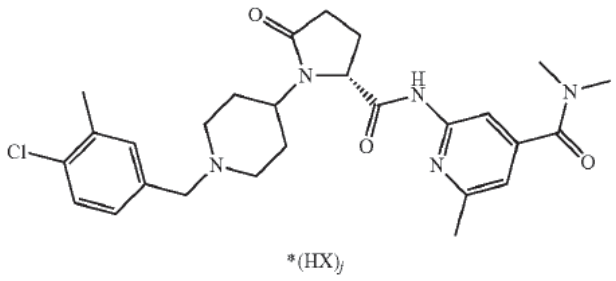
R^{2b} is H, $CONR^{2b.1}R^{2b.2}$;

$R^{2b.1}$ is C_{1-4}-haloalkyl;

$R^{2b.2}$ is H, C_{1-4}-alkyl.

12. The use of the compound or a salt thereof claim 1, wherein the compound is a co-crystal of the formula according to claim ~~8~~9, wherein $R^{2b.1}$ and $R^{2b.2}$ are together a C_{3-6}-alkylene group forming with the nitrogen atom a heterocyclic ring, wherein optionally one carbon atom or the ring is replaced by an oxygen atom.

13. The use of the compound or a salt thereof of claim 1, wherein the compound is a co-crystal having the formula shown below,

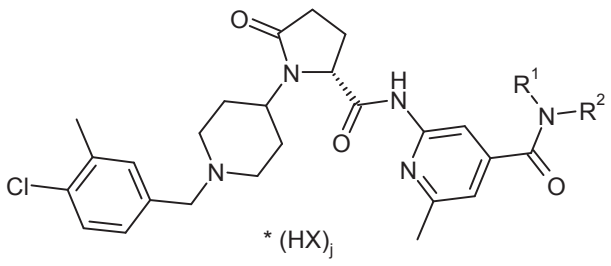


wherein j is 0,

and the co-crystal former is selected from the group consisting of L-(+)-ascorbic acid, mucic acid, pamoic acid, nicotinic acid, succinamide, nicotinamide, isonicotinamide, L-lysine, and L-proline.

14. The use of a pharmaceutical composition comprising the compound or a salt thereof of claim 1~~,~~ in the manufacture of a medicament for treating a skin disorder selected from pruritus, xerosis, and Bullous pemphigoid (BP), wherein the pharmaceutical

composition comprises as an active ingredient one or more compounds of the formula 2 below,



2

wherein

R^1 is H, C_{1-6}-alkyl, C_{0-4}-alkyl-C_{3-6}-cycloalkyl, C_{1-6}-haloalkyl;

R^2 is H, C_{1-6}-alkyl;

X is an anion selected from the group consisting of chloride or ½ dibenzoyltartrate

j is 1 or 2,

and wherein the pharmaceutical composition further comprises a first diluent, a second diluent, a binder, a disintegrant and a lubricant.

15. The use of the compound or a salt thereof of claim 1 in the manufacture of a medicament for treating pruritus.

16. The use of the compound or a salt thereof of claim 1 in the manufacture of a medicament for treating xerosis.

17. The use of the compound or a salt thereof of claim 1 in the manufacture of a medicament for treating BP.