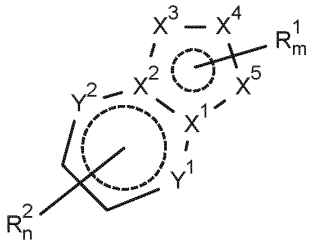
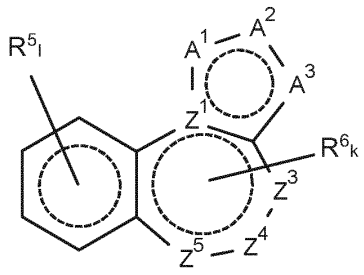
Claims

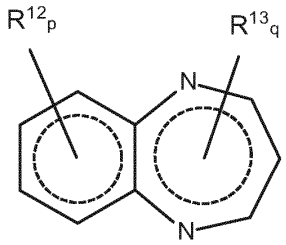
1. A compound for use in the treatment of itch, wherein the compound comprises the general formula (1a), general formula (1b) or general formula (Ic),



(1a),



(1b),



(Ic), in particular formula (1a) and (1b), more particular (1a), wherein

- X^1, X^2, X^3, X^4 and X^5 are independently from each other –C, -N, -S or -O wherein at least two of X^1, X^2, X^3, X^4 and X^5 are -N,
- Y^1 and Y^2 are independently from each other -C or -N,
- m of R^1_m is 1,
- R^1 is an unsubstituted phenyl, a phenyl substituted with C_1-C_4-alkyl, F, Cl, Br, I, -CN, a substituted or unsubstituted biphenyl or –(C=O)-R^3, with R^3 being a substituted or unsubstituted aryl or 5- to 6-membered heteroaryl, in particular a C_6 aryl or 6-membered heteroaryl, more particularly a 6-membered heteroaryl,
- n of R^2_n is 1 or 2,
- each R^2 independently from any other R^2 is a substituted or unsubstituted C_3-C_8 cycloalkyl, a substituted or unsubstituted C_1-C_6 alkyl, a substituted or unsubstituted C_1-C_6 alcohol, a substituted or unsubstituted 6-membered heteroaryl, a halogen, particularly -F, or –O-CH_2-R^4, with R^4 being a substituted or unsubstituted 5- or 6-membered heteroaryl, in particular a 5-membered heteroaryl,
- Z^1, Z^3, Z^4 and Z^5 are independently of each other –C, –N, -S or –O, in particular Z^1 is -C or -N and Z^3 and Z^4 are –C, –N, -S or –O,

- A^1 and A^2, are independently of each other –C, -N or –(C=O)-O-$R^{7'}$ and A^3 is –(C=O)-O-$R^{7'}$, with $R^{7'}$ being an C_1-C_6-alkyl, in particular A^1 and A^2 are independently of each other –C or -N and A^3 is –(C=O)-O-$R^{7'}$, with $R^{7'}$ being an C_1-C_6-alkyl, in particular a C_1-C_2-alkyl, more particularly a C_2-alkyl,
- l of R^5_l is 1 or 2
- each R^5 is independently from each other a C_1-C_4 alkinyl or a halogen,
- k of R^6_k is 1, 2, 3 or 4, in particular 1 or 2,
- each R^6 is independently from each other a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1-C_3 alkyl, oxygen or hydrogen, in particular a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1-C_3 alkyl, more particularly a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl,
- p of R^{12} is 1 or 2, in particular 1,
- R^{12} is independently from each other a substituted or unsubstituted C_1-C_4-alkyl, I, Br, Cl or F,
- q of R^{13} is 1, 2, 3 or 4,
- R^{13} is independently from each other a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1-C_3 alkyl, oxygen or hydrogen.

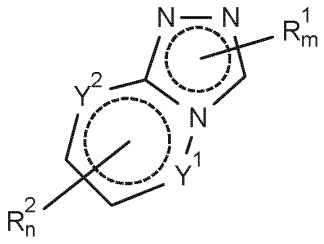
2. The compound for use in the treatment of itch according to claim 1, provided that the compound is a positive allosteric α2 and/or α3 $GABA_A$ receptor modulator.

3. The compound for use in the treatment of itch according to claims 1 or 2, wherein the compound comprises the general formula (1a), general formula (1b) or general formula (Ic), in particular formula (1a) and (1b), more particular (1a), wherein
   - X^1, X^2, X^3, X^4 and X^5 are independently from each other –C or -N, wherein at least two of X^1, X^2, X^3, X^4 and X^5 are -N,
   - Y^1 and Y^2 are independently from each other -C or -N,
   - m of R^1_m is 1,
   - R^1 is an unsubstituted phenyl, a phenyl substituted with C_1-C_4-alkyl, F, Cl, Br, I, -CN, a substituted or unsubstituted biphenyl or –(C=O)-R^3, with R^3 being a substituted or unsubstituted aryl or 5- to 6-membered heteroaryl, in particular a C_6 aryl or 6-membered heteroaryl, more particularly a 6-membered heteroaryl,
   - n of R^2_n is 1 or 2,
   - each R^2 independently from any other R^2 is a substituted or unsubstituted C_3-C_8 cycloalkyl, a substituted or unsubstituted C_1-C_6 alkyl, a substituted or

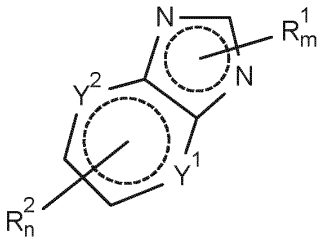
unsubstituted C_1-C_6 alcohol, a substituted or unsubstituted 6-membered heteroaryl, a halogen, particularly -F, or –O-CH_2-R^4, with R^4 being a substituted or unsubstituted 5- or 6-membered heteroaryl, in particular a 5-membered heteroaryl,

- Z^1 , Z^3, Z^4 and Z^5 are independently of each other –C, or –N,
- A^1 and A^2 are independently of each other –C or -N and A^3 is –(C=O)-O-$R^{7'}$, with $R^{7'}$ being a C_1-C_4-alkyl, in particular a C_1-C_2-alkyl, more particularly a C_2-alkyl,
- l of R^5_l is 1 or 2
- each R^5 is independently from each other a C_1-C_4 alkinyl or a halogen,
- k of R^6_k is 1, 2, 3 or 4, in particular 1 or 2
- each R^6 is independently from each other a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1-C_3 alkyl, oxygen or hydrogen, in particular a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1-C_3 alkyl, more particularly a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl,
- p of R^{12} is 1,
- R^{12} is a substituted or unsubstituted C_1-C_4-alkyl, I, Br, Cl or F,
- q of R^{13} is 1, 2, 3 or 4,
- R^{13} is independently from each other a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1-C_3 alkyl, oxygen or hydrogen.

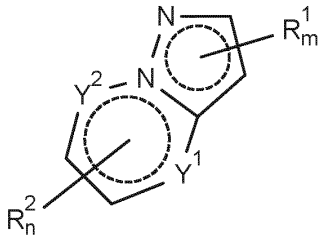
4. The compound according to any one of claim 1 to 3, wherein the compound comprises the general formula (2), (3), (4), (5), (Ic) or (7), in particular (2), (3), (4), (5) or (7), more particularly (2), (3), (4) or (5),



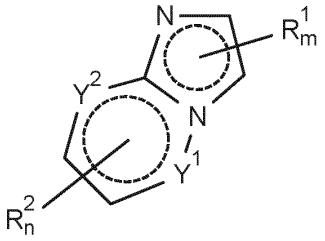
(2),



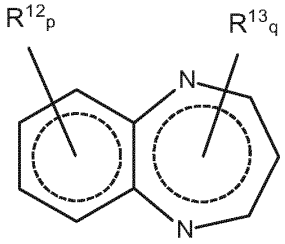
(3),



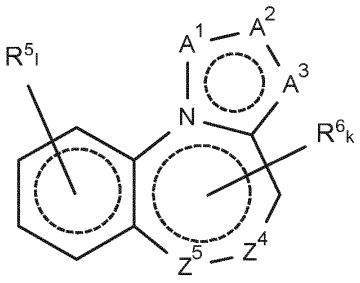
(4),



(5),



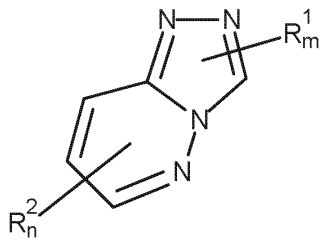
(Ic),



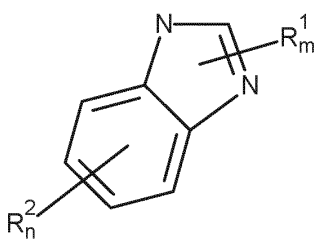
(7),

with Y^1, Y^2, Z^4, Z^5, m of $R^1{}_m$, R^1, R^3, n of $R^2{}_n$, R^2, R^4, p of $R^{12}{}_p$, R^{12}, q of $R^{13}{}_q$, R^{13}, l of $R^5{}_l$, R^5, k of $R^6{}_k$, R^6, A^1, A^2 and A^3 having the same meaning as defined above.

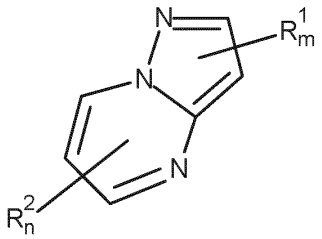
5. The compound according to any one of claims 1 to 4, wherein the compound comprises the general formula (2a), (3a), (4a), (5a), (5b), (Ic) or (7a), in particular (2a), (3a), (4a), (5a), (5b) or (7a), more particularly (2a), (3a), (4a), (5a) or (5b),



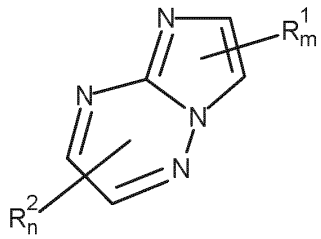
(2a),



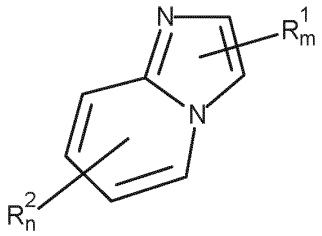
(3a),



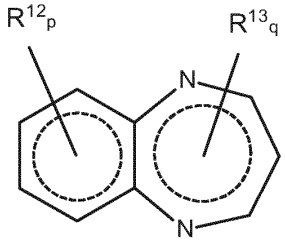
(4a),



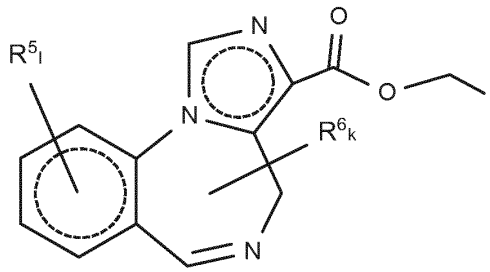
(5a),



(5b),



(Ic),



or (7a),

with m of $R^1{}_m$, R^1, R^3, n of $R^2{}_n$, R^2, R^4, p of R^{12}, R^{12}, q of R^{13}, R^{13}, l of $R^5{}_l$, R^5, k of $R^6{}_k$ and R^6 having the same meaning as defined above.

6. The compound according to any one of claims 1 to 5, wherein
   - m of R^1 is 1 and R^1 is:
     - an unsubstituted phenyl,
     - a substituted phenyl comprising C_1-C_4-alkyl, F, Cl, Br, I, -CN as substituents, wherein in particular said substituted phenyl comprises at least one -F as a substituent,
     - an unsubstituted biphenyl,
     - a substituted biphenyl comprising at least one -CN as a substituent, particularly on the phenyl moiety not connected to the parent moiety, or
     - a substituted biphenyl comprising at least one -CN as a substituent, particularly on the phenyl moiety not connected to the parent moiety, wherein in particular one phenyl moiety comprises additionally at least one -F as a substituent, more

particularly each phenyl moiety comprises additionally at least one -F as a substituent, or

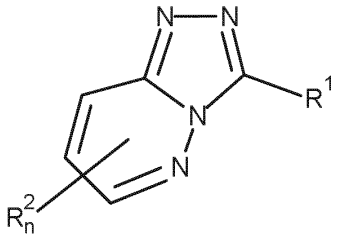
- –(C=O)-R^3, with R^3 being pyridine.

7. The compound according to any one of claims 1 to 6, wherein
   - n of R^2 is 1 or 2 and R^2 is
     - an unsubstituted C_3-C_8 cycloalkyl, particularly a C_4-cycloalkyl,
     - an unsubstituted C_1-C_6 alkyl, particularly tert-butyl, or
     - -O-CH_2-R^4, with R^4 being a substituted or unsubstituted 5-membered heteroaryl, in particular R^4 being a substituted or unsubstituted triazole,
     - an unsubstituted C_1-C_6 alcohol, in particular a C_3 alcohol, more particularly isopropanol,
     - a halogen, in particular -F,
     - an unsubstituted 6-membered heteroaryl, in particular pyridine.
8. The compound according to any one of claims 1 to 7, wherein
   - n of R^2 is 2 and
     - one R^2 is
       - an unsubstituted C_3-C_8 cycloalkyl, particularly a C_4-cycloalkyl, or
       - an unsubstituted C_1-C_6 alkyl, particularly tert-butyl, and
     - the other R^2 is
       - O-CH_2-R^4, with R^4 being a substituted or unsubstituted 5-membered heteroaryl, in particular a substituted or unsubstituted triazole, or
     - one R^2 is
       - an unsubstituted C_1-C_6 alcohol, in particular a C_3 alcohol, more particularly isopropanol, and
     - the other R^2 is

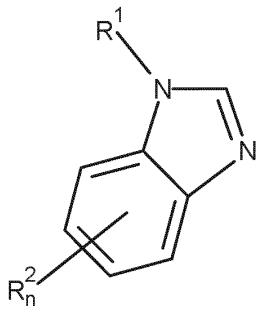
   a halogen, in particular -F.
9. The compound according to any one of claims 1 to 7, wherein n of R^2 is 1 and R^2 is an unsubstituted C_1-C_6 alcohol, in particular a C_3 alcohol, or an unsubstituted 6-membered heteroaryl, in particular pyridine, wherein in particular R^2 is a C_3 alcohol, more particularly isopropanol.
10. The compound according to any one of the preceding claims, wherein
    - l of R^5 is 1 and R^5 is
      - I, Cl, Br, F, in particular -I, or
      - a C_2 alkinyl.
11. The compound according to any one of the preceding claims, wherein k of R^6 is 1 and R^6 is a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a

substituted or unsubstituted C_1-C_3 alkyl, in particular a substituted or unsubstituted C_6 aryl, a 5- to 6-membered substituted or unsubstituted heteroaryl, more particularly a phenyl, a phenyl substituted with F or Cl, thiophen or pyridine.

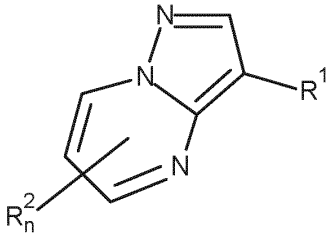
12. The compound according to any one of claims 1 to 11, wherein the compound comprises the general formula (2a'), (3a'), (4a'), (5a'), (5b'), (VI) or (7a'), in particular (2a'), (3a'), (4a'), (5a'), (5b') or (7a'), even more particularly (2a'), (3a'), (4a'), (5a') or (5b'),



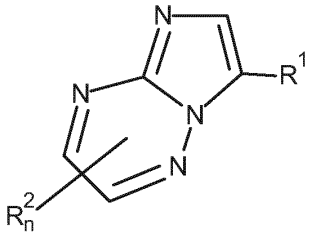
(2a'),



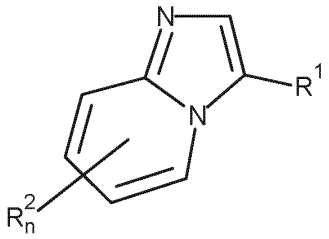
(3a'),



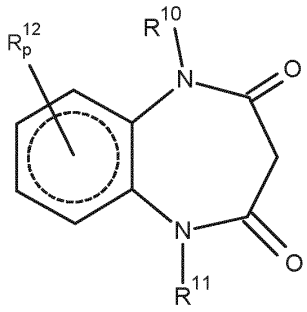
(4a'),



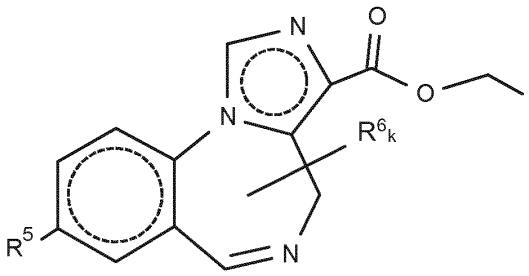
(5a'),



(5b'),



(VI),



or (7a'), wherein

- R^{10} is a substituted or unsubstituted aryl, a substituted or unsubstituted C_1-C_3 alkyl or hydrogen, in particular hydrogen,
- R^{11} is a substituted or unsubstituted aryl, a substituted or unsubstituted C_1-C_3 alkyl, or hydrogen, in particular a substituted or unsubstituted aryl, more particularly phenyl,
- p of R^{12} is 1 and R^{12} is I, Br, Cl or F, in particular Cl,
- with R^1, R^3, n of $R^2{}_n$, R^2, R^4, R^{10}, R^{11}, p of R^{12}, R^{12}, R^5, k of $R^6{}_k$ and R^6 having the same meaning as defined above.

13. The compound according to any one of claims 1 to 12, wherein the compound comprises the general formula (2a'), (3a'), (4a'), (5a'), (5b'), (VI) or (7a'), in particular (2a'), (3a'), (4a'), (5a'), (5b') or (7a'), even more particularly (2a'), (3a'), (4a'), (5a') or (5b'),

wherein

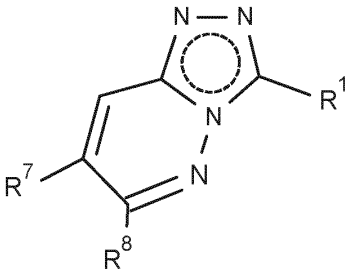
- R^1 is
  - in case of formula (2a')
    - a substituted or unsubstituted C_6 aryl, in particular
      - an unsubstituted phenyl,
      - a substituted phenyl comprising C_1-C_4-alkyl, F, Cl, Br, I, -CN as substituents, wherein in particular said substituted phenyl comprises at least one -F as a substituent,
  - in case of formula (3a'), (5a') or (5b'),
    - a substituted or unsubstituted biphenyl, in particular
      - an unsubstituted biphenyl,
      - a substituted biphenyl comprising at least one -CN as a substituent, particularly on the phenyl moiety not connected to the parent moiety, wherein in particular one phenyl moiety comprises additionally at least one -F as a substituent, more particularly each phenyl moiety comprises additionally at least one -F as a substituent, or
  - in case of formula (4a'),

- –(C=O)-R^3, with R^3 being a substituted or unsubstituted C_6 heteroaryl, in particular
  - with R^3 being pyridine,

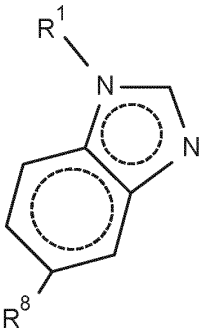
- R^5 is
  - in case of formula (7a')
    - C_2 alkinyl or I, in particular a C_2 alkinyl,

wherein $R^2{}_n$, R^{10}, R^{11} and $R^{12}{}_p$ and $R^6{}_k$ have the same meaning as defined above.

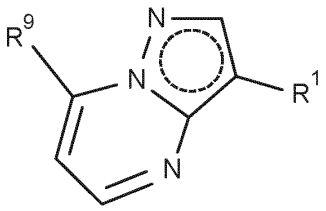
14. The compound according to any one of claims 1 to 13, wherein the compound comprises the general formula (2a''), (3a''), (4a''), (5a''), (5b''), (VIa'') or (7a''), in particular (2a''), (3a''), (4a''), (5a''), (5b'') or (7a''), more particularly (2a''), (3a''), (4a''), (5a'') or (5b''),



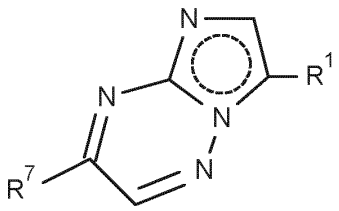
(2a''),



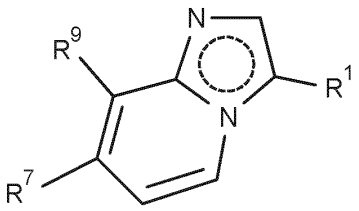
(3a''),



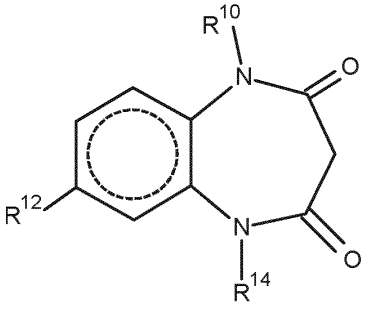
(4a''),



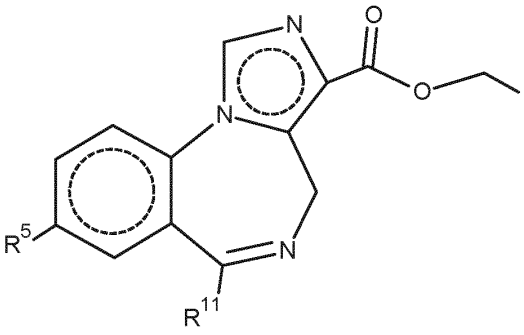
(5a''),



(5b''),



(VIa'') or



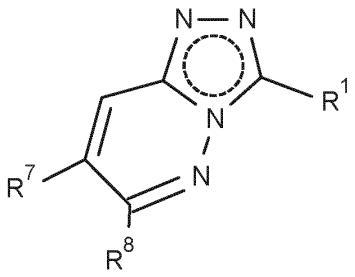
(7a'')

with R^1 having the same meaning as defined above, and

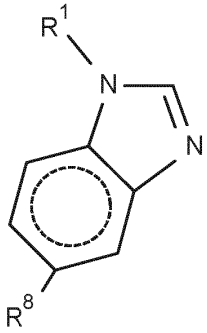
- R^7 being
  - an unsubstituted C_1-C_6 alkyl, particularly tert-butyl,
  - an unsubstituted C_3-C_8 cycloalkyl, particularly a C_4-cycloalkyl,
  - an unsubstituted C_1-C_6 alcohol, in particular a C_3 alcohol, in particular
    - R^7 being in case of formula (2a'')
      - an unsubstituted C_1-C_6 alkyl, particularly tert-butyl, or
      - an unsubstituted C_3-C_8 cycloalkyl, particularly a C_4-cycloalkyl, or
    - R^7 being in case of formula (5a'') or (5b'')
      - an unsubstituted C_1-C_6 alcohol, in particular a C_3 alcohol,
- R^8 being
  - $-O-CH_2-R^4$, with R^4 being a substituted or unsubstituted 5-membered heteroaryl, in particular a substituted or unsubstituted triazole, or
  - an unsubstituted C_1-C_6 alcohol, in particular a C_3 alcohol, in particular
    - R^8 being in case of formula (2a'')
      $-O-CH_2-R^4$, with R^4 being a substituted or unsubstituted 5-membered heteroaryl, in particular a substituted or unsubstituted triazole, or
    - R^8 being in case of formula (3a'')
      - an unsubstituted C_1-C_6 alcohol, in particular a C_3 alcohol,

- R^9 being
  - an unsubstituted C_6 heteroaryl, in particular pyridine, or
  - a halogen, in particular -F,
    - R^9 being in case of formula (4a'')
      - an unsubstituted 6-membered heteroaryl, in particular pyridine, or
    - R^9 being in case of formula (5b'')
      - a halogen, in particular –F,
- R^{10} being
  - a C_1-C_3 alkyl or hydrogen, in particular hydrogen
- R^{11} being a substituted or unsubstituted aryl or heteroaryl, in particular pyridine, thiophene, a phenyl or a phenyl substituted with F or Cl,
- R^{14} being a substituted or unsubstituted aryl or heteroaryl, in particular a substituted or unsubstituted aryl, more particularly phenyl
- R^{12} being I, Cl, Br or F, in particular Cl,
- R^5 being C_2 alkinyl or I, in particular C_2 alkinyl.

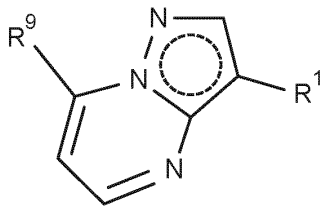
15. The compound according to any one of claims 1 to 14, wherein the compound comprises the general formula (2a''), (3a''), (4a''), (5a'') or (5b'')



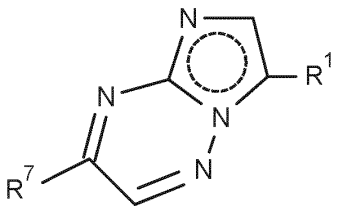
(2a''),



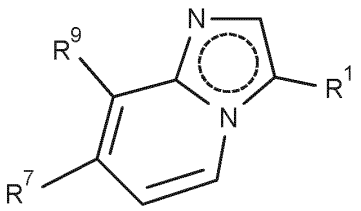
(3a''),



(4a''),



(5a'') or



(5b''),

with

- in case of formula (2a'')
  - R^1 being
    - an unsubstituted phenyl,
    - a substituted phenyl comprising C_1-C_4-alkyl, F, Cl, Br, I, -CN as substituents, wherein in particular said substituted phenyl comprises at least one -F as a substituent,
  - R^7 being
    - an unsubstituted C_1-C_6 alkyl, particularly tert-butyl, or
    - an unsubstituted C_3-C_8 cycloalkyl, particularly a C_4-cycloalkyl, and
  - R^8 being
    - -O-CH_2-R^4, with R^4 being a substituted or unsubstituted 5-membered heteroaryl, in particular a substituted or unsubstituted triazole,
- in case of formula (3a'')
  - R^1 being
    - an unsubstituted biphenyl,
    - a substituted biphenyl comprising at least one -CN as a substituent, particularly on the phenyl moiety not connected to the parent moiety, or
    - a substituted biphenyl comprising at least one -CN as a substituent, particularly on the phenyl moiety not connected to the parent moiety, wherein in particular one phenyl moiety comprises additionally at least one -F as a substituent, more particularly each phenyl moiety comprises additionally at least one -F as a substituent,
  - wherein in particular R^1 being
    - a substituted biphenyl comprising at least one -CN as a substituent, particularly on the phenyl moiety not connected to the parent moiety,

- R^8 being
  - an unsubstituted C_1-C_6 alcohol, in particular a C_3 alcohol, more particularly isopropanol,
- in case of formula (4a'')
  - R^1 being
    - –(C=O)-R^3, with R^3 being an unsubstituted 6-membered heteroaryl, in particular R^3 being pyridine, and
  - R^9 being
    - being an unsubstituted C_6 heteroaryl, in particular pyridine,
- in case of formula (5a'')
  - R^1 being
    - an unsubstituted biphenyl,
    - a substituted biphenyl comprising at least one -CN as a substituent, particularly on the phenyl moiety not connected to the parent moiety, wherein in particular one phenyl moiety comprises additionally at least one -F as a substituent, more particularly each phenyl moiety comprises additionally at least one -F as a substituent,
  - wherein in particular R^1 being
    - a substituted biphenyl comprising at least one -CN as a substituent, particularly on the phenyl moiety not connected to the parent moiety, wherein in particular one phenyl moiety comprises additionally at least one -F as a substituent, more particularly each phenyl moiety comprises additionally at least one -F as a substituent,
  - R^7 being
    - an unsubstituted C_1-C_6 alcohol, in particular a C_3 alcohol, more particularly isopropanol,
- in case of formula (5b'')
  - R^1 being
    - an unsubstituted biphenyl,
    - a substituted biphenyl comprising at least one -CN as a substituent, particularly on the phenyl moiety not connected to the parent moiety, wherein in particular one phenyl moiety comprises additionally at least one -F as a substituent, more particularly each phenyl moiety comprises additionally at least one -F as a substituent,

- wherein in particular R^1 being
  - a substituted biphenyl comprising at least one -CN as a substituent, particularly on the phenyl moiety not connected to the parent moiety, wherein in particular one phenyl moiety comprises additionally at least one -F as a substituent, more particularly each phenyl moiety comprises additionally at least one -F as a substituent,
- R^7 being
  - an unsubstituted C_1-C_6 alcohol, in particular a C_3 alcohol, more particularly isopropanol,
- R^9 being
  - a halogen, in particular -F.

16. The compound according to any one of claims 1 or 15 for use in preventing Serotonin-, Histamine-, Chloroquine-, Compound48/80 (CAS NO. 94724-12-6)- and bile acid-induced itch, in particular Serotonin-, Chloroquine-, Compound48/80- and bile acid-induced itch, more particularly Serotonin-induced itch.
17. The compound according to any one of claims 1 or 15 for use in the treatment of itch in an animal.
18. A positive allosteric α2 or α3 $GABA_A$ receptor modulator for use in the treatment of itch, in particular a modulator according to any one of the claims 1 to 15.