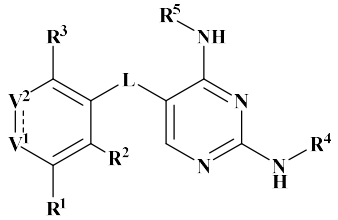
WHAT IS CLAIMED IS:

Claim 1. Use of a compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof in the manufacture of a medicament for treating, suppressing or alleviating cough or cough impulse:



Formula (I)

wherein:

L is selected from the group consisting of C(=O), CRR', NR, O, S, S=O and $S(=O)_2$;

V^1 is selected from the group consisting of N, $\overset{\oplus}{N}—\overset{\ominus}{O}$ and NR;

V^2 is selected from the group consisting of CR^6 and C(=O);

--- represents either a single bond or a double bond, provided that when --- is a single bond, V^1 is NR and V^2 is C(=O);

R and R' are each independently selected from the group consisting of H, halogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, saturated or partially unsaturated C_{3-10} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl and C_{6-12} aralkyl, and at most 2 ring members in the cyclic hydrocarbyl and heterocyclyl are C(=O);

R^1, R^2, R^3 and R^6 are each independently selected from the group consisting of H, halogen, -CN, $-NO_2$, $-NH_2$, -OH, -SH, -Se-R, $-Si(R)_3$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, saturated or partially unsaturated C_{3-10} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl, C_{6-12} aralkyl, C_{1-6} haloalkyl, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^a$, $-OR^a$, $-SR^a$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^b$, $-S(=O)(=NR)R^a$, $-NR^aR^b$, $-C(=O)NR^aR^b$, $-C(=S)NR^aR^b$, $-C(=NR)NR^aR^b$, $-NR^a-C(=O)R^b$, $-NR^a-C(=O)OR^b$, $-NR^a-S(=O)_2-R^b$, $-NR^a-C(=O)-NR^aR^b$, $-C_{1-6}$ alkylene-NR^aR^b, $-C_{1-6}$ alkylene-OR^a, $-C_{1-6}$ alkylene-C(=O)R, $-C_{1-6}$ alkenylene-OR^a, -O-C_{1-6} alkylene-NR^aR^b and $-P(=O)R^aR^b$;

R^4 and R^5 are each independently selected from the group consisting of H, $-C(=O)OR^a$, $-NR^aR^b$, $-NR^a-C(=O)R^b$, $-NR^a-C(=O)OR^b$, $-C_{1-6}$ alkylene-NR^aR^b, $-C_{1-6}$ alkylene-OR^a, $-C_{1-6}$ alkylene-O-C_{1-6} alkylene-OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, saturated or partially unsaturated C_{3-10} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl and C_{6-12} aralkyl;

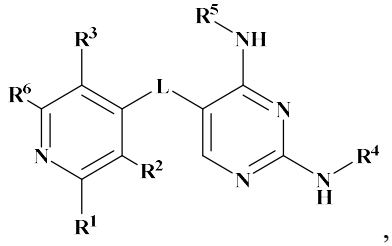
alternatively, R^1 and R^4 together form $-NHCH_2CH_2-O-CH_2CH_2-$;

the above alkyl, alkylene, alkenyl, alkynyl, cyclic hydrocarbyl, heterocyclyl, aryl, heteroaryl and aralkyl, at each occurrence, are each optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxyl, oxo, amino, cyano, nitro, $-Si(R)_3$, C_{1-6} alkyl, saturated or partially unsaturated C_{3-6} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl, C_{6-12} aralkyl, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^a$, $-OR^a$, $-SR^a$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^b$, $-NR^aR^b$, $-C(=O)NR^aR^b$, $-NR^a-C(=O)R^b$, $-NR^a-C(=O)OR^b$, $-NR^a-S(=O)_2-R^b$, $-NR^a-C(=O)-NR^aR^b$, $-C_{1-6}$ alkylene-NR^aR^b, $-C_{1-6}$ alkylene-OR^a, $-C_{1-6}$ alkenylene-OR^a and -O-C_{1-6} alkylene-NR^aR^b, the alkyl, cyclic hydrocarbyl, heterocyclyl, aryl, heteroaryl and aralkyl are further optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxyl, oxo, amino, cyano, nitro, $-NR^aR^b$, C_{1-6} alkyl, -O-C_{1-6} alkyl, saturated or partially unsaturated C_{3-6} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl and C_{6-12} aralkyl; and

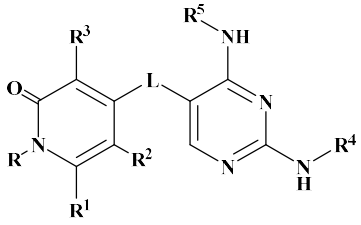
R^a and R^b, at each occurrence, are each independently selected from the group consisting of H, -OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, saturated or partially unsaturated C_{3-10} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl and C_{6-12} aralkyl; alternatively, R^a and R^b together with the atom to which they are attached form a 3- to 12-membered heterocycle or heteroaromatic ring, the above groups are further optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxyl, oxo, amino, cyano, nitro, C_{1-6} alkyl, -O-C_{1-6} alkyl, saturated or partially unsaturated C_{3-6} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl

and C_{6-12} aralkyl.

Claim 2. The use according to claim 1, wherein the compound has the structure of any of the following formulae:

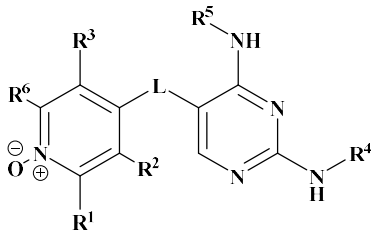


(II)



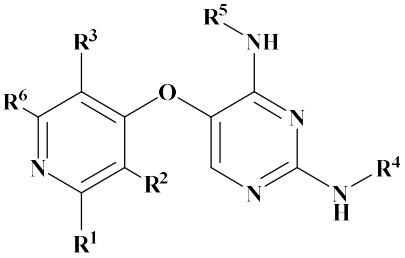
(III)

or

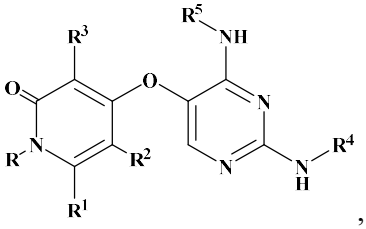


(IV);

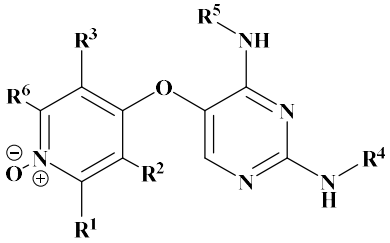
Claim 3. The use according to claim 1 or 2, wherein the compound has the structure of any of the following formulae:



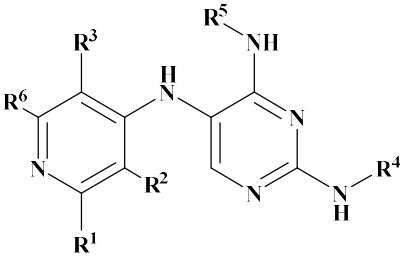
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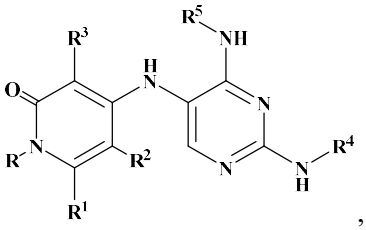
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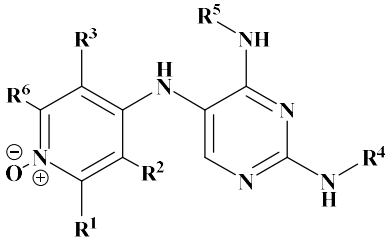
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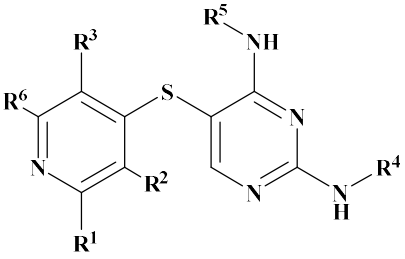
(II'')



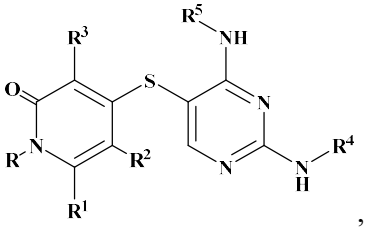
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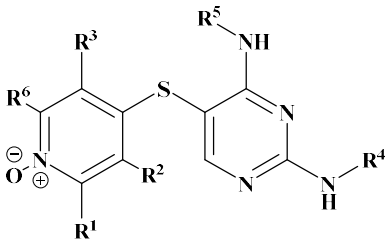
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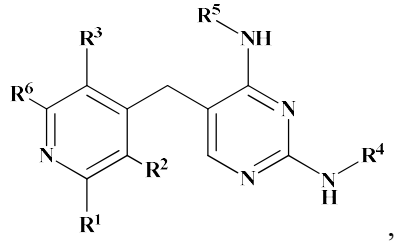
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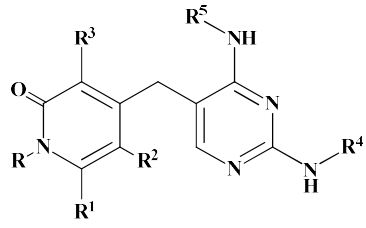
(III''')



(IV''')

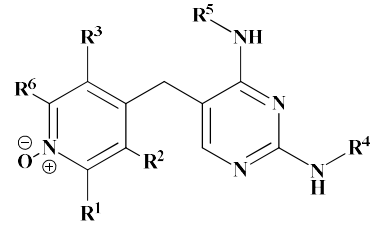


(II'''')



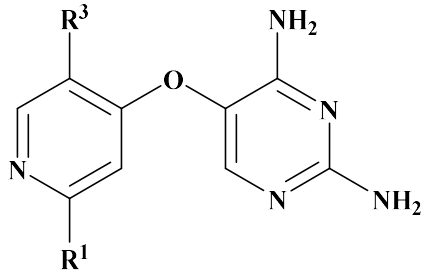
(III'''')

or



(IV'''');

Claim 4. The use according to any one of claims 1 to 3, wherein the compound of Formula (I) has the structure of any of the following formulae:



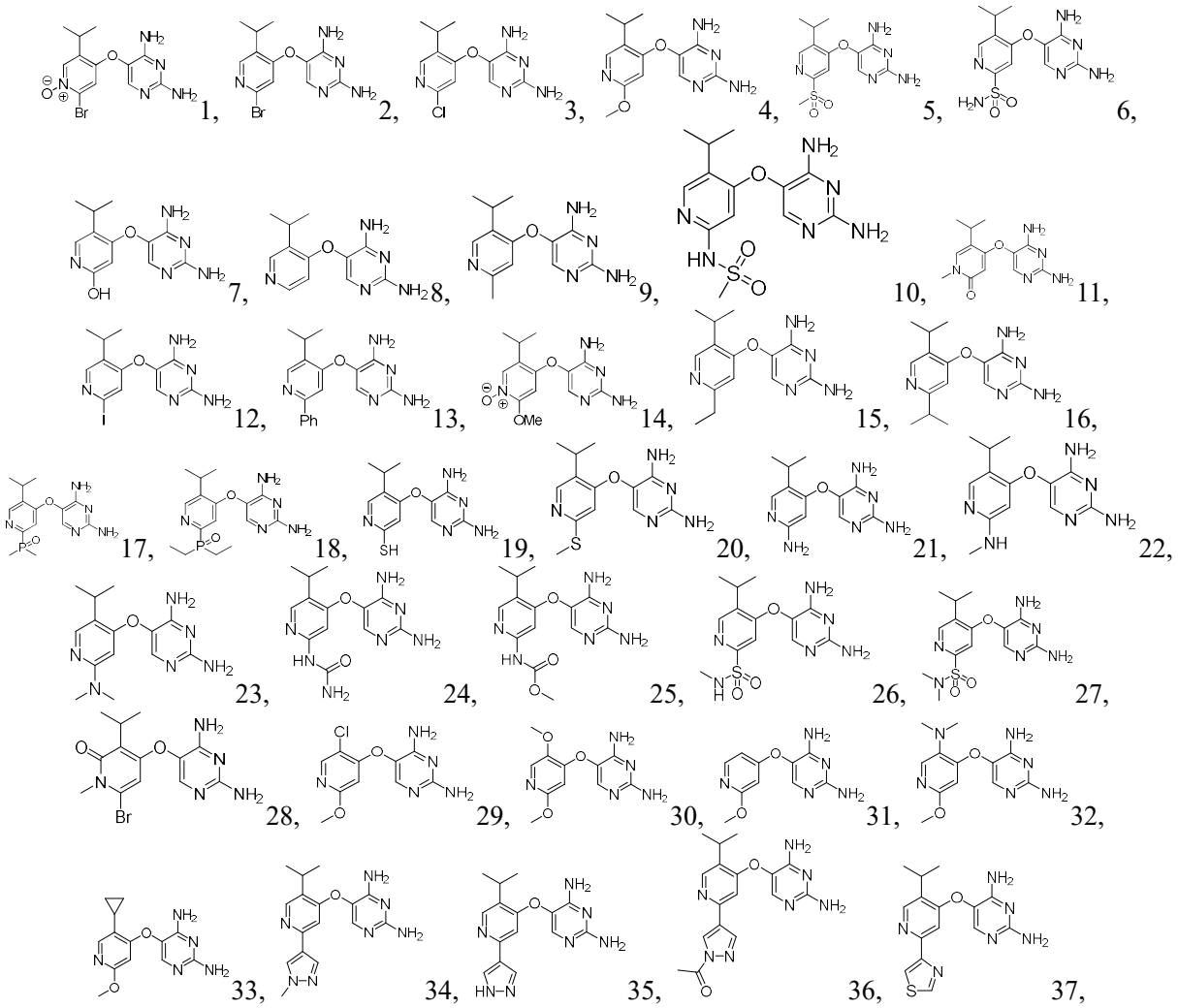
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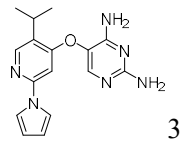
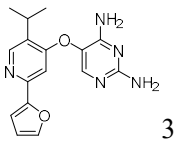
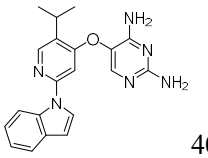
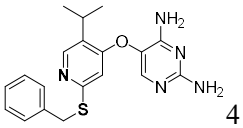
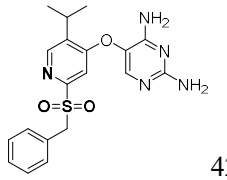
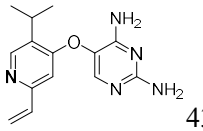
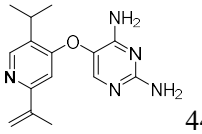
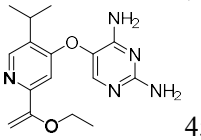
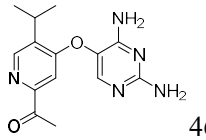
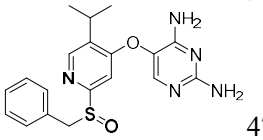
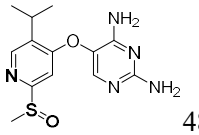
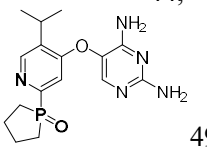
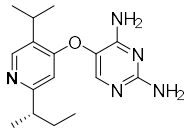
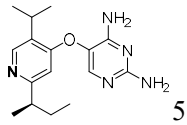
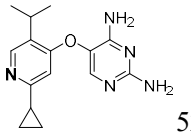
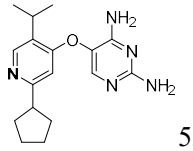
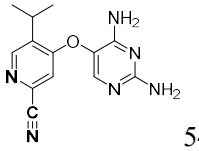
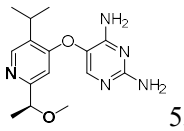
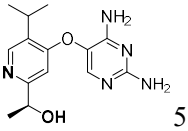
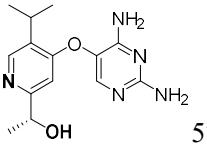
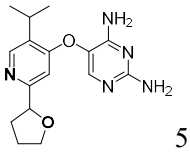
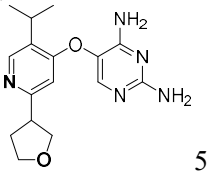
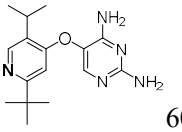
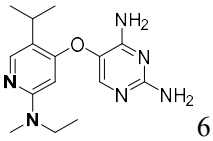
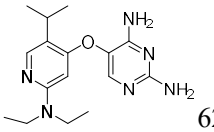
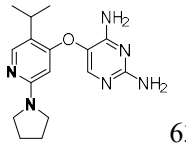
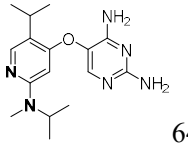
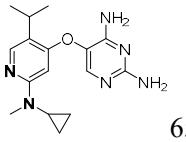
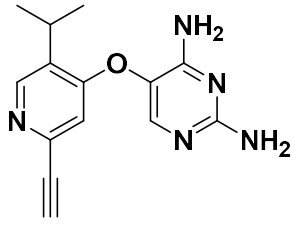
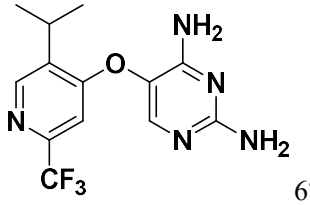
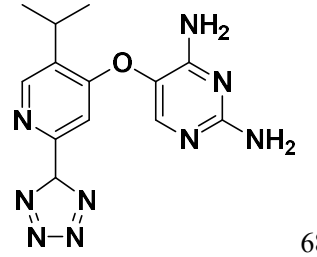
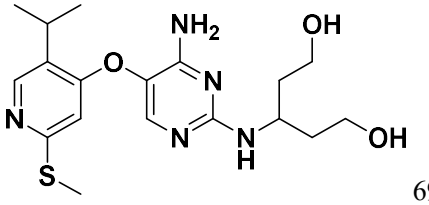
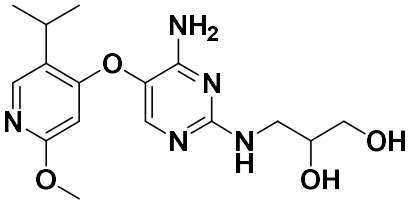
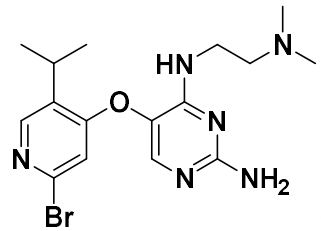
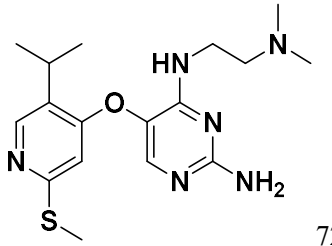
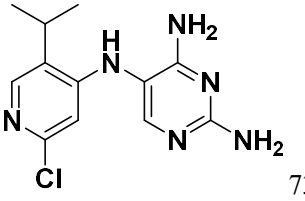
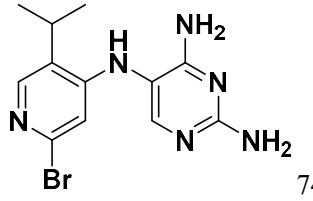
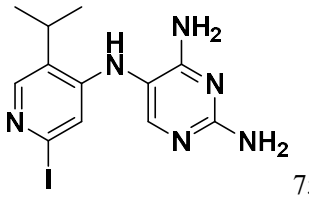
wherein:
R^1 is selected from the group consisting of F, Cl, Br, I and C_{2-6} alkynyl; and
R^3 is C_{1-6} alkyl, preferably isopropyl.

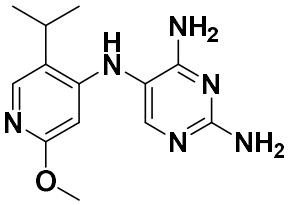
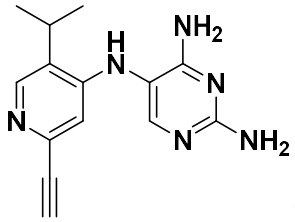
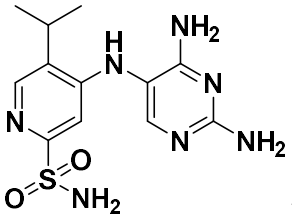
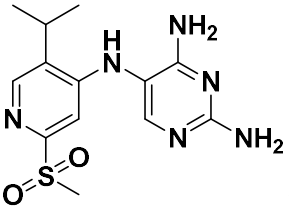
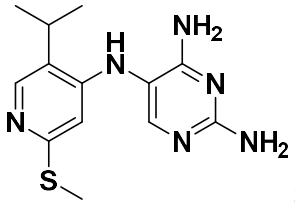
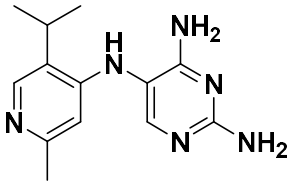
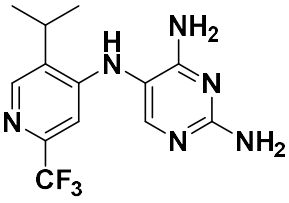
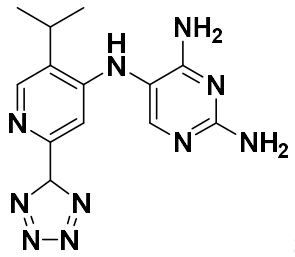
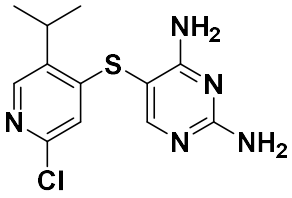
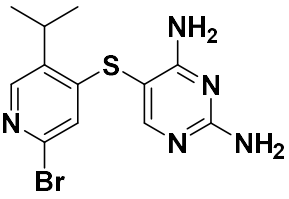
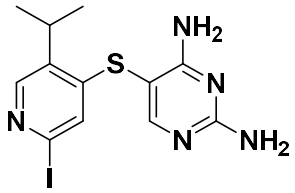
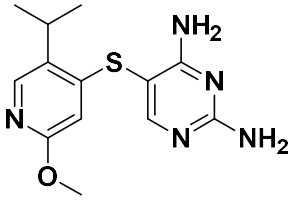
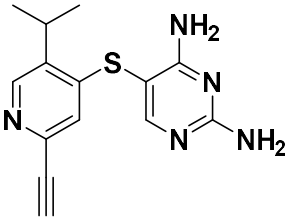
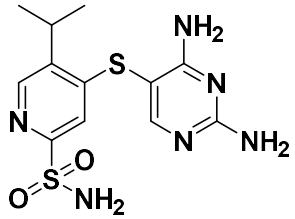
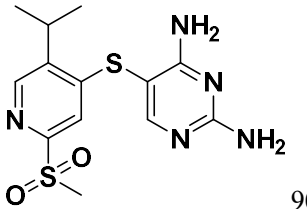
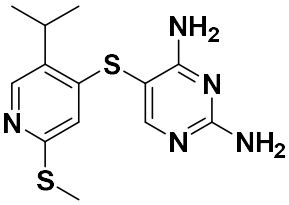
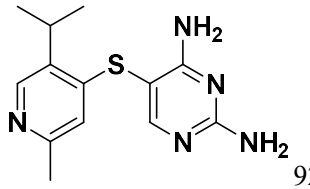
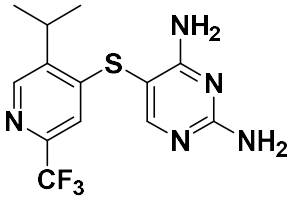
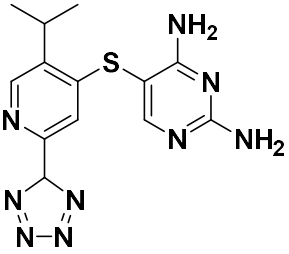
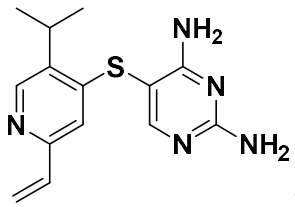
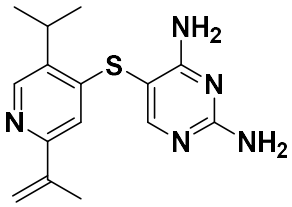
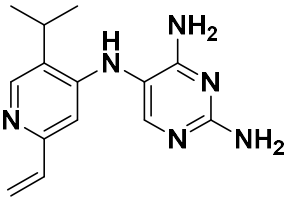
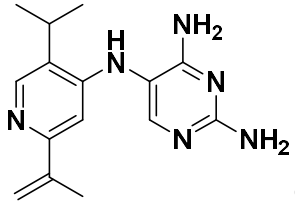
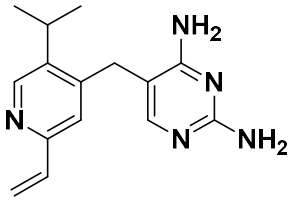
Claim 5. The use according to any one of claims 1 to 4, wherein R^1 is Br or ethynyl.

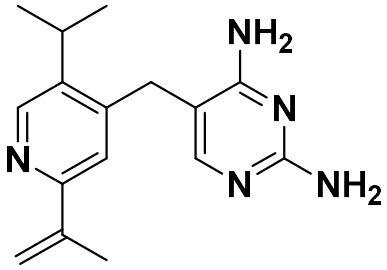
Claim 6. The use according to any one of claims 1 to 5, wherein R^3 is isopropyl.

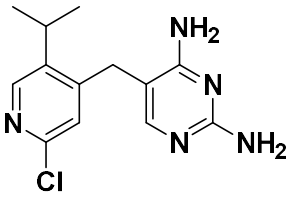
Claim 7. The use according to any one of claims 1 to 6, wherein the compound has the following structure:

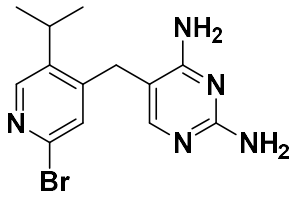


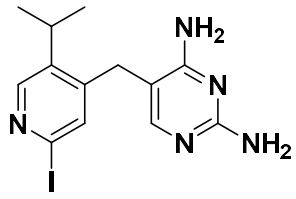

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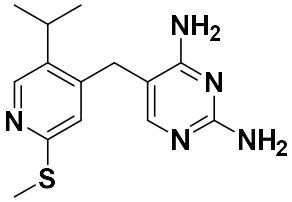

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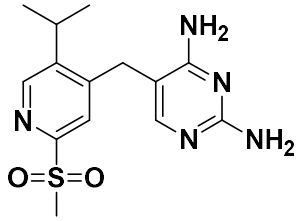


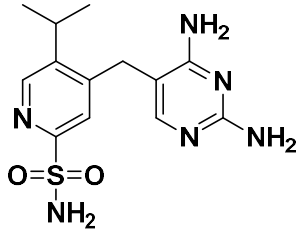
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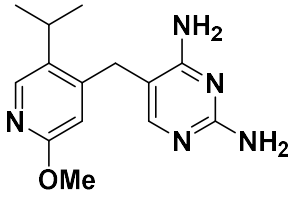
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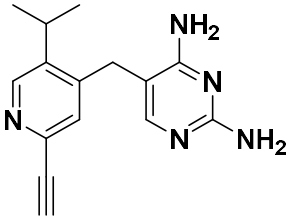
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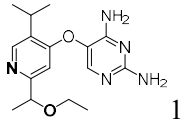
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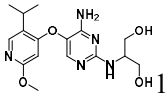
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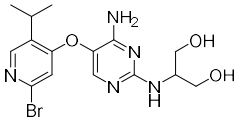
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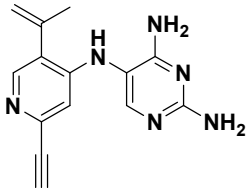
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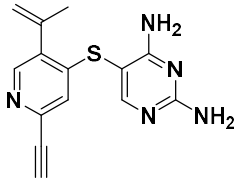
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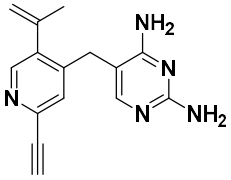
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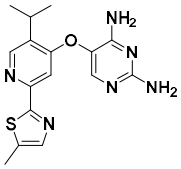
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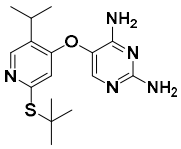
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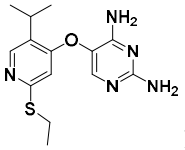
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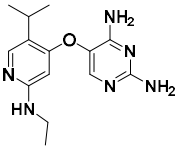
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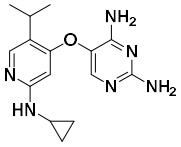
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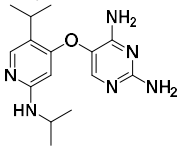
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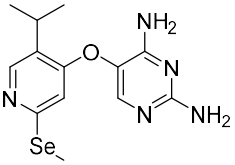
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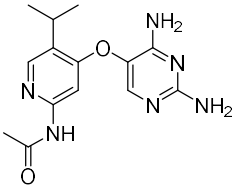
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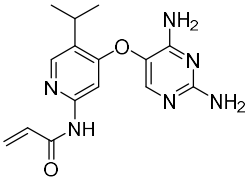
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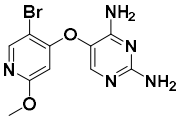
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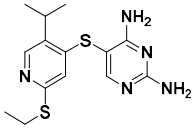
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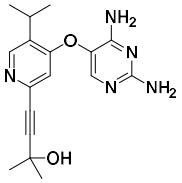
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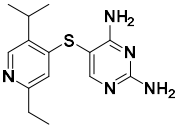
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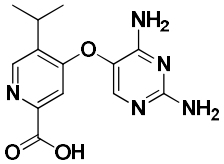
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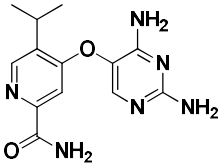
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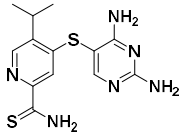
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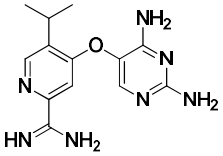
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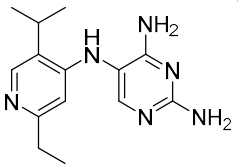
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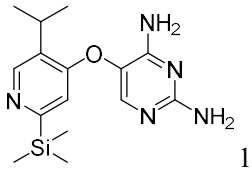
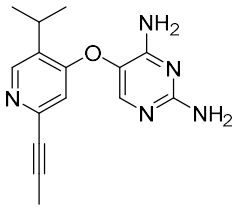
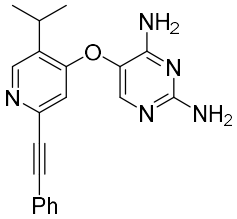
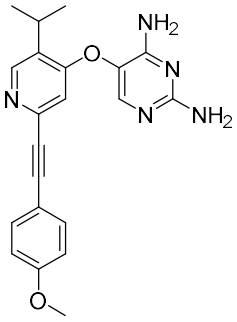
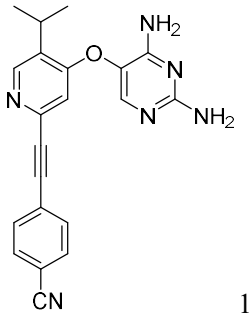
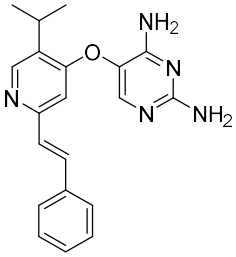
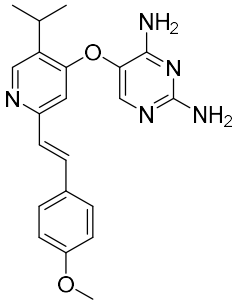
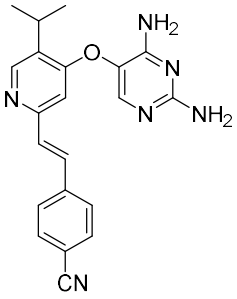
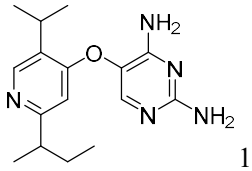
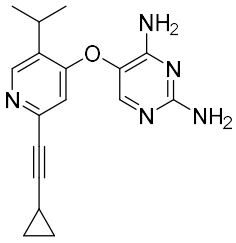
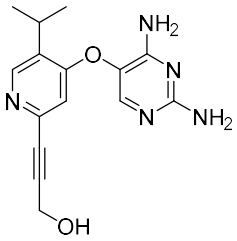
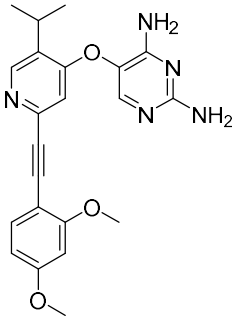
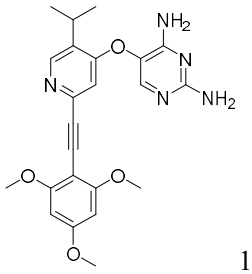
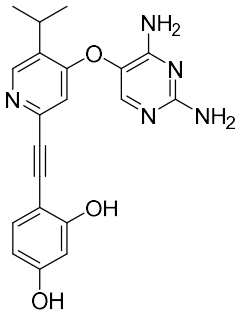
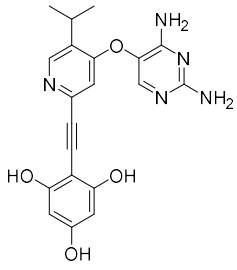
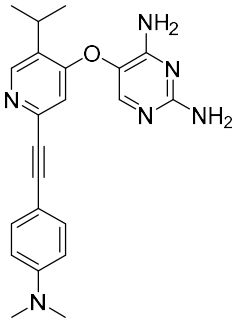
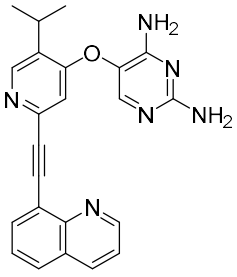
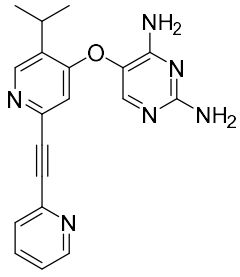
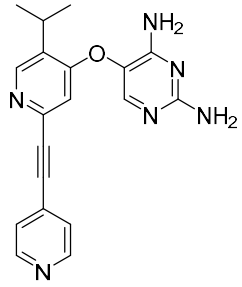
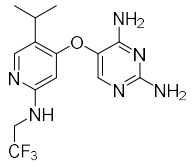
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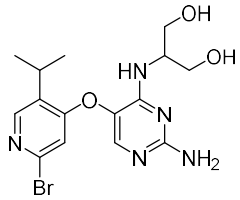
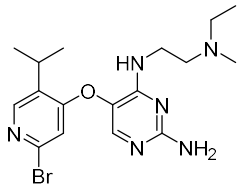
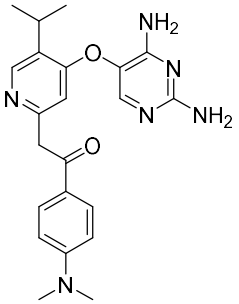
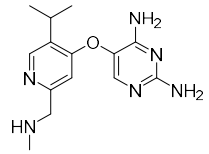
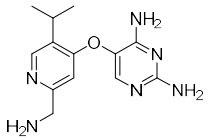
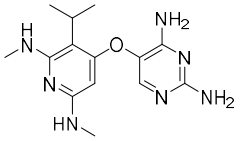
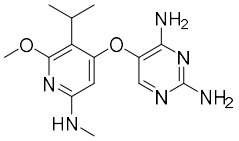
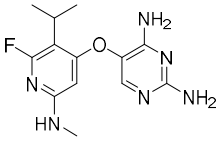
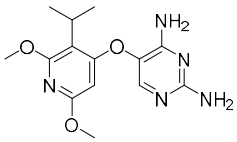
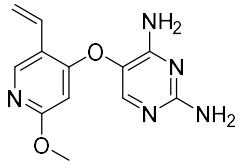
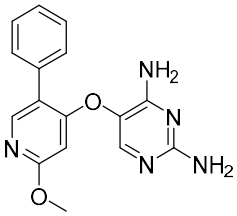
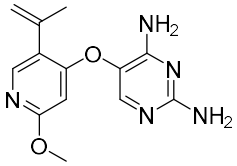
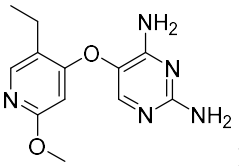
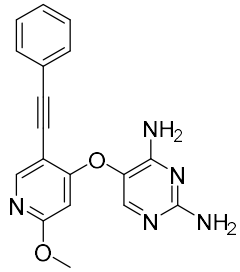
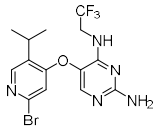
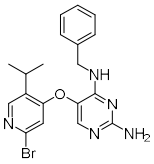
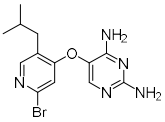
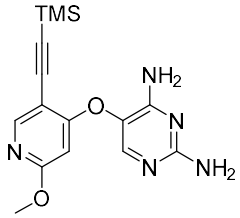
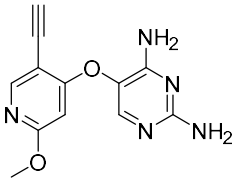
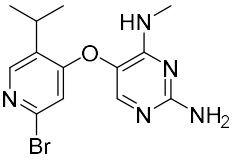
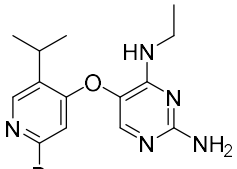
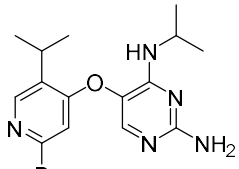
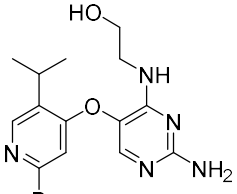
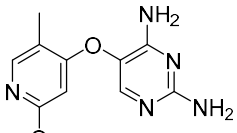
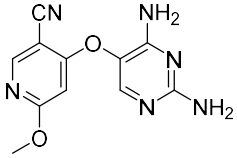
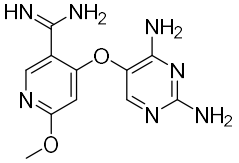
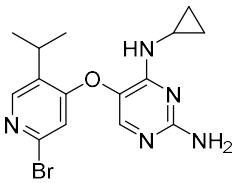
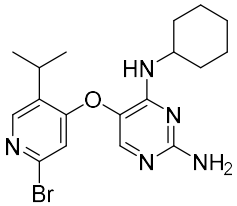
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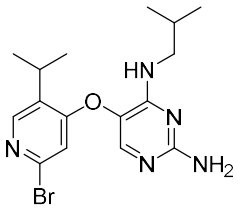
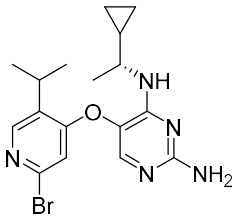
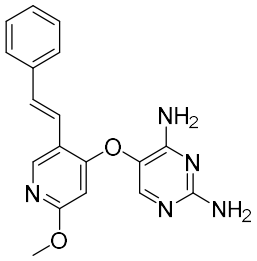
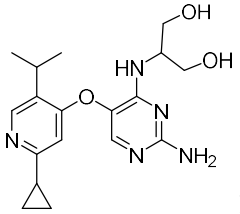
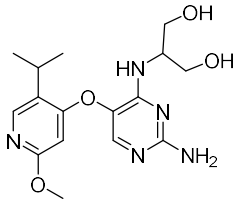
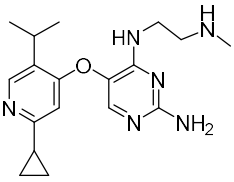
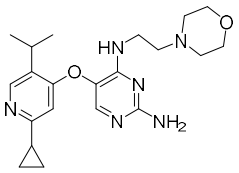
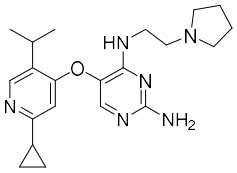
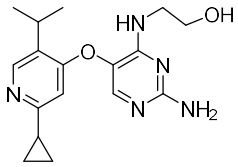
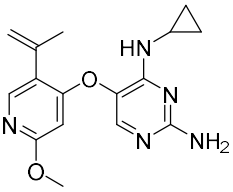
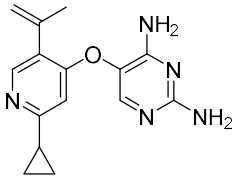
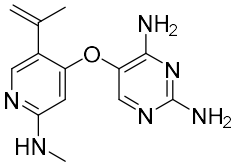
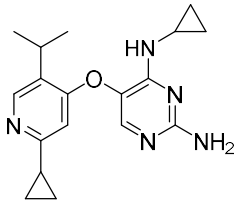
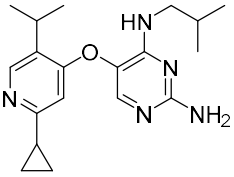
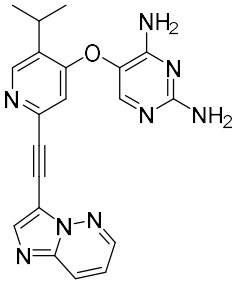
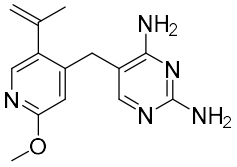
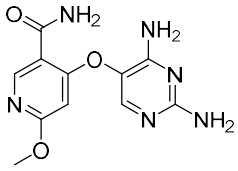
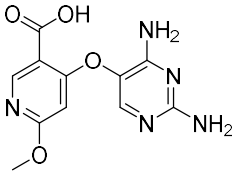
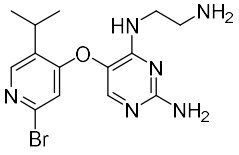
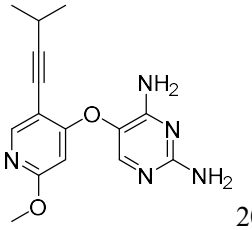
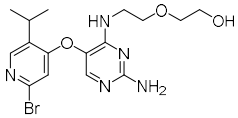
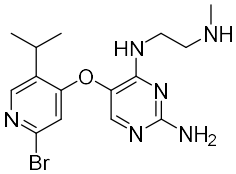
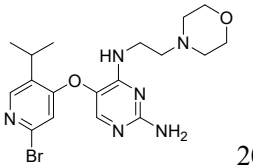
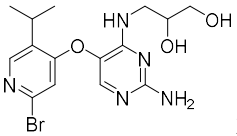
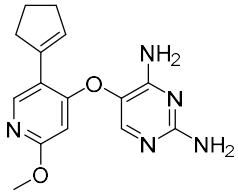
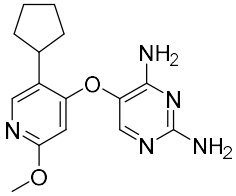
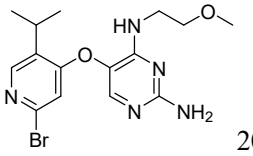
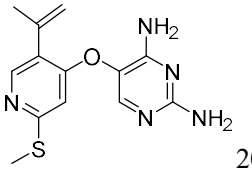
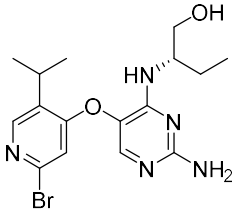
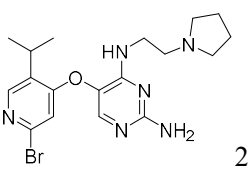
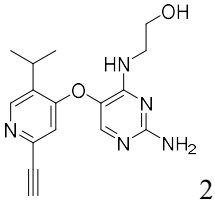
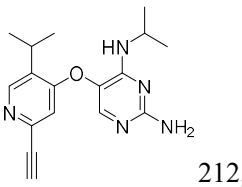
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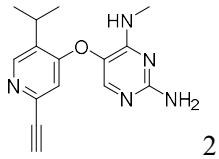
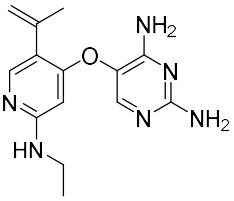
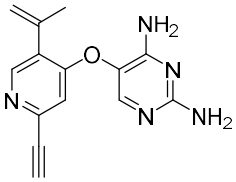
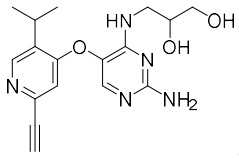
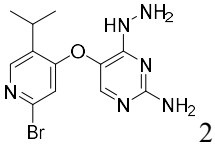
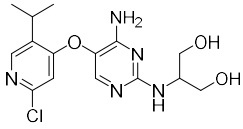
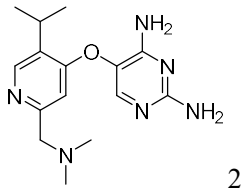
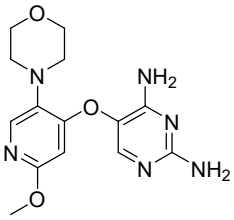
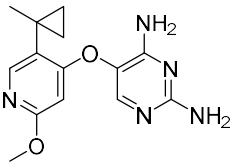
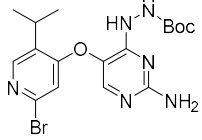
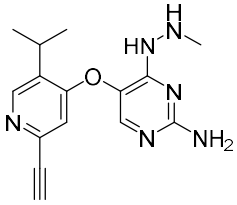
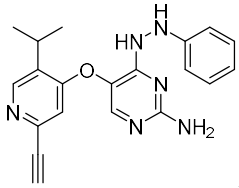
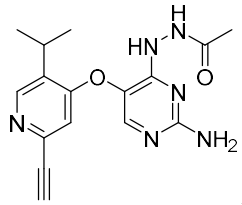
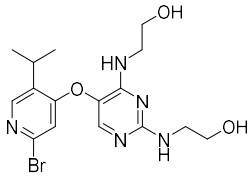
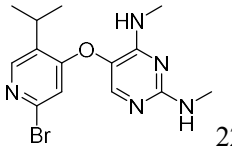
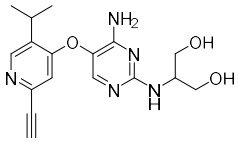
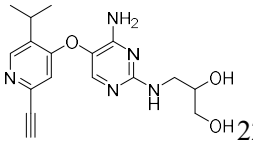
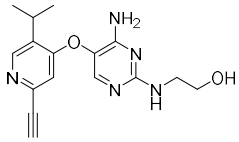
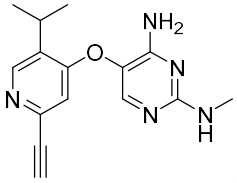
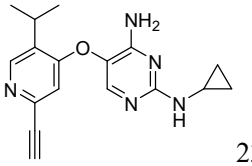
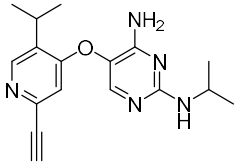
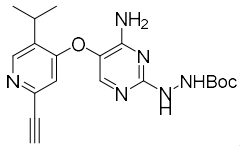
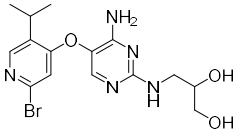
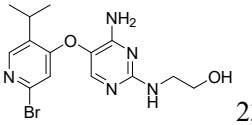
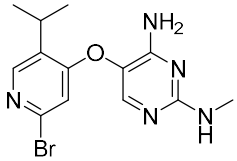
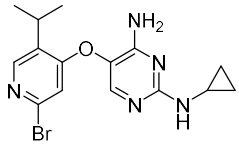
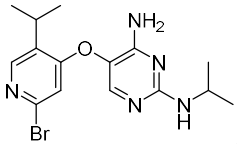
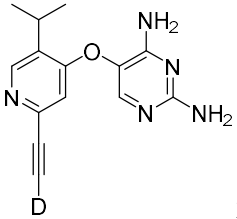
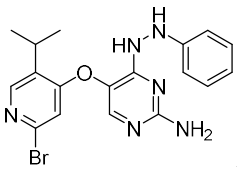
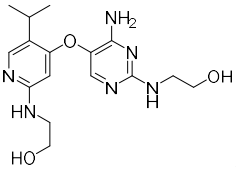
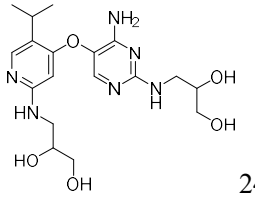
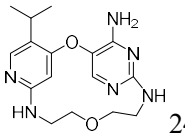
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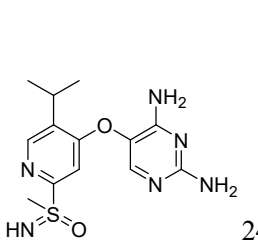
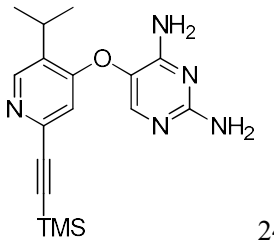
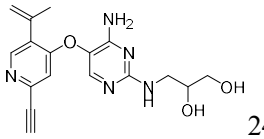
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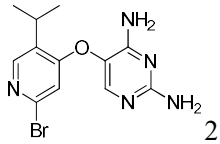
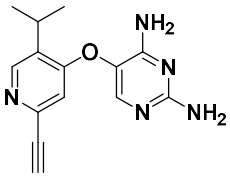

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245, TMS 246 or  247.

Claim 8. The use according to any one of claims 1 to 7, wherein the compound has the following structure:


2, or  66.

Claim 9. The use according to any one of claims 1 to 8, wherein the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound, thereof is to be administered in an amount of 0.005 mg/day to 5000 mg/day, e.g., in an amount of 0.005, 0.05, 0.5, 5, 10, 20, 30, 40, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500 or 5000 mg/day.

Claim 10. The use according to any one of claims 1 to 8, wherein the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof is to be administered in an amount of 1 ng/kg to 200 mg/kg, 1 µg/kg to 100 mg/kg or 1 mg/kg to 50 mg/kg per day, e.g., is to be administered in an amount of 1 µg/kg, 10 µg/kg, 25 µg/kg, 50 µg/kg, 75 µg/kg, 100 µg/kg, 125 µg/kg, 150 µg/kg, 175 µg/kg, 200 µg/kg, 225 µg/kg, 250 µg/kg, 275 µg/kg, 300 µg/kg, 325 µg/kg, 350 µg/kg, 375 µg/kg, 400 µg/kg, 425 µg/kg, 450 µg/kg, 475 µg/kg, 500 µg/kg, 525 µg/kg, 550 µg/kg, 575 µg/kg, 600 µg/kg, 625 µg/kg, 650 µg/kg, 675 µg/kg, 700 µg/kg, 725 µg/kg, 750 µg/kg, 775 µg/kg, 800 µg/kg, 825 µg/kg, 850 µg/kg, 875 µg/kg, 900 µg/kg, 925 µg/kg, 950 µg/kg, 975 µg/kg, 1 mg/kg, 5 mg/kg, 10 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, 30 mg/kg, 35 mg/kg, 40 mg/kg, 45 mg/kg, 50 mg/kg, 60 mg/kg, 70 mg/kg, 80 mg/kg, 90 mg/kg, 100 mg/kg, 125 mg/kg, 150 mg/kg, 175 mg/kg, 200 mg/kg body weight per unit dose.

Claim 11. The use according to any one of claims 1 to 10, wherein the daily dose of the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof is to be administered at one time or is to be administered in two, three or four doses.

Claim 12. The use according to any one of claims 1 to 11, wherein the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof is to be administered continuously for at least 3 days, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, at least 17 days, at least 18 days, at least 19 days, at least 20 days, at least 21 days, at least 22 days, at least 23 days, at least 24 days, at least 25 days, at least 30 days, at least 35 days, at least 40 days, at least 45 days, at least 50 days, at least half a year, at least 1 year, at least 2 years, at least 3 years, at least 4 years, or at least 5 years.

Claim 13. The use according to any one of claims 1 to 12, wherein the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof is to be administered for one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) courses of treatment, wherein each course of treatment lasts for at least 3 days, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, at least 17 days, at least 18 days, at least 19 days, at least 20 days, at least 21 days, at least 22 days, at least 23 days, at least 24 days, at least 25 days, at least 30 days, at least 35 days, at least 40 days, at least 45 days or at least 50 days; and the interval between

every two courses of treatment is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days, two weeks, three weeks, or four weeks.

Claim 149. The use according to any one of claims 1 to 13, wherein the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof is to be administered through injection (e.g., intravenous, intraarterial, subcutaneous, intraperitoneal, intramuscular injection, including dripping), or transdermal administration, or is to be administered via oral, buccal, nasal, transmucosal, or topical route, as an ophthalmic formulation, or via inhalation.

Claim 15. The use according to any one of claims 1 to 14, wherein the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof is to be administered in a dosage form selected from the group consisting of tablet, capsule, lozenge, hard candy, powder, spray, emulsion, cream, salve, suppository, gel, paste, lotion, injection, nanoformulation, patch, aqueous suspension, solution, elixir, and syrup.

Claim 16. The use according to any one of claims 1 to 15, wherein the cough is selected from the group consisting of acute cough, sub-acute cough, chronic cough, treatment-resistant cough, treatment-resistant chronic cough, idiopathic chronic cough, post-viral cough, iatrogenic cough, cough associated with post-nasal drip, cough associated with cold, upper respiratory infection, asthma, lung cancer and/or chronic obstructive pulmonary disease (COPD), cough associated with interstitial disease, cough associated with pulmonary fibrosis, cough associated with gastroesophageal reflux disease (GERD), cough associated with smoking or a form of bronchitis, and neuronal hypersensitivity underlying acute, sub-acute or chronic cough.

Claim 17. The use according to any one of claims 1 to 16, wherein the cough is selected from the group consisting of chronic cough, treatment-resistant cough, treatment-resistant chronic cough, and cough associated with pulmonary fibrosis.