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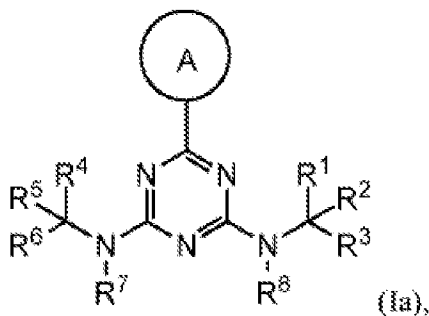
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HR P20200274 T1

PATENTNI ZAHTEVI

1. Spoj koji ima formulu Ia ili njegova farmaceutske prihvatljiva sol ili hidrat, naznačen time što:



prsten A je izabran od fenila, pirazolila, oksazolila, izoksazolila, piridinila, pirimidinila, pirazinila i tiazolila, pri čemu je prsten A izbornu supstituiran sa do dva supstituenta nezavisno izabrana od halo, -C₁-C₄ alkila, -C₁-C₄ haloalkila, -C₁-C₄ hidroksialkila, -NH-S(O)₂-(C₁-C₄ alkil), -S(O)₂NH(C₁-C₄ alkil), -CN, -S(O)₂-(C₁-C₄ alkil), C₁-C₄ alkoksi, -NH(C₁-C₄ alkil), -OH, -OCF₃, -CN, -NH₂, -C(O)NH₂, -C(O)NH(C₁-C₄ alkil), -C(O)-N(C₁-C₄ alkil)₂ i ciklopropila izbornu supstituiranog sa OH;

R¹, R³, R⁴ i R⁶ su svaki nezavisno izabrani od vodika, C₁-C₄ alkila, C₁-C₄ haloalkila, -O-C₁-C₄ alkila i CN, pri čemu je svaka navedena alkil grupa od R¹, R³, R⁴, i R⁶ nezavisno izbornu supstituirana sa -OH, -NH₂, -CN, -O-C₁-C₄ alkil, -NH(C₁-C₄ alkil) ili -N(C₁-C₄ alkil)₂;

R² i R⁵ su svaki nezavisno izabrani od: -(C₁-C₆ alkil), -(C₁-C₆ alkil)-C(O)-NH₂, -(C₁-C₆ alkil)-CO₂H, -(C₂-C₆ alkenil ili alkinil), -(C₁-C₆ alkilen)-O-(C₁-C₆ alkil), -(C₀-C₆ alkilen)-C(O)N(R⁶)-(C₁-C₆ alkil) i -(C₀-C₆ alkilen)-C(O)-(C₁-C₆ alkil) gdje: svaka alkil ili alkilen grupa prisutna u R² i R⁵ je izbornu supstituirana s jednim ili više -OH, -O(C₁-C₄ alkil), -CO₂H ili halo;

svaka terminalna metil grupa prisutna u R² i R⁵ je izbornu zamijenjena sa -CH₂OH, CF₃, -CH₂F, -CH₂Cl, C(O)CH₃, C(OCF₃), CN ili CO₂H;

R⁷ i R⁸ su svaki nezavisno izabrani od vodika i C₁-C₆ alkila; gdje

R¹ i R² su izbornu uzeti zajedno tako da formiraju karbociklil ili heterociklil od kojih je bilo koji izbornu supstituiran sa do 3 supstituenta nezavisno izabrana od halo, npr., fluoro, C₁-C₄ alkila, C₁-C₄ haloalkila, C₁-C₄ alkoksi, -CN, =O, -OH, arila, heteroarila, -SO₂C₁-C₄ alkila, -CO₂C₁-C₄ alkila, -C(O)arila i -C(O)C₁-C₄ alkila; ili R⁴ i R⁵ su izbornu uzeti zajedno tako da formiraju karbociklil ili heterociklil od kojih je bilo koji izbornu supstituiran sa do 3 supstituenta nezavisno izabrana od halo, npr., fluoro, C₁-C₄ alkila, C₁-C₄ haloalkila, C₁-C₄ alkoksi, -CN, =O, -OH, arila, heteroarila, -SO₂C₁-C₄ alkila, -CO₂C₁-C₄ alkila, -C(O)arila i -C(O)C₁-C₄ alkila; gdje:

(i) kada je A jednak piridil izbornu supstituiran kao što je opisano u prethodnom tekstu, tada (A) N(R⁷)C(R⁴)(R⁵)(R⁶) i N(R⁸)C(R¹)(R²)(R³) nisu oba NHCH₂CH₂OH, ili NH-cikloheksil, i (B) kada je N(R⁷)C(R⁴)(R⁵)(R⁶) jednak NHC(CH₃)₃, tada N(R⁸)C(R¹)(R²)(R³) nije NH-CH₂CH₃;

(ii) kada je A jednak pirazolil, oksazolil, izoksazolil, piridinil, pirimidinil, pirazinil ili tiazolil izbornu supstituiran kao što je opisan u prethodnom tekstu, tada N(R⁷)C(R⁴)(R⁵)(R⁶) i N(R⁸)C(R¹)(R²)(R³) nisu oba N(CH₂CH₃)₂, NHCH₂CH₂-i-propil ili NHCH₂CH(CH₃)₂;

(iii) kada je A jednak 1-pirazolil izbornu supstituiran kao što je opisano u prethodnom tekstu, tada ni N(R⁷)C(R⁴)(R⁵)(R⁶) ni N(R⁸)C(R¹)(R²)(R³) nisu NH-izopropil, NHCH₂CH₃, ili N(CH₂CH₃)₂,

(iv) kada je A jednako fenil izbornu supstituiran kao što je opisano u prethodnom tekstu, tada N(R⁷)C(R⁴)(R⁵)(R⁶) nije isti kao N(R⁸)C(R¹)(R²)(R³),

(v) spoj nije: N²-izopropil-6-fenil-N⁴-(tetrahydro-2H-piran-4-il)-1,3,5-triazin-2,4-diamin.

2. Spoj ili njegova farmaceutske prihvatljiva sol ili hidrat prema patentnom zahtjevu 1, naznačeno time što prsten A je izbornu supstituiran sa do dva supstituenta nezavisno izabrana od halo, -C₁-C₄ alkila, -C₁-C₄ haloalkila, -C₁-C₄ hidroksialkila, -NH-S(O)₂-(C₁-C₄ alkil), -S(O)₂NH(C₁-C₄ alkil), -CN, -S(O)₂-(C₁-C₄ alkil), C₁-C₄ alkoksi, -NH(C₁-C₄ alkil), -OH, -CN i -NH₂.

3. Spoj ili njegova farmaceutske prihvatljiva sol ili hidrat prema patentnom zahtjevu 1, naznačen time što:

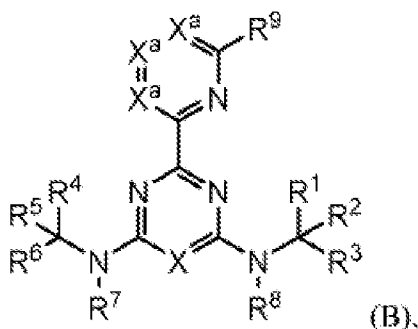
R¹, R³, R⁴ i R⁶ su svaki nezavisno izabrani od vodika, C₁-C₄ alkila, C₁-C₄ haloalkila, -O-C₁-C₄ alkila i CN, pri čemu je svaka navedena alkil grupa od R¹, R³, R⁴ i R⁶ nezavisno izbornu supstituirana sa -OH, -NH₂, -CN, -O-C₁-C₄ alkilom, -NH(C₁-C₄ alkil) ili -N(C₁-C₄ alkil)₂;

R² i R⁵ su svaki nezavisno izabrani od: -(C₁-C₆ alkil), -(C₁-C₆ alkil)-C(O)-NH₂, -(C₁-C₆ alkil)-CO₂H, -(C₂-C₆ alkenil ili alkinil), -(C₁-C₆ alkilen)-O-(C₁-C₆ alkil), -(C₀-C₆ alkilen)-C(O)N(R⁶)-(C₁-C₆ alkil) i -(C₀-C₆ alkilen)-C(O)-(C₁-C₆ alkil), gdje:

bilo koja alkil ili alkilen grupa prisutna u R² i R⁵ je izbornu supstituirana jednim ili više -OH, -O(C₁-C₄ alkil), -CO₂H ili halo;

bilo koja terminalna grupa prisutna u R² i R⁵ je izbornu zamijenjena sa -CH₂OH, CF₃, -CH₂F, -CH₂Cl, C(O)CH₃, C(OCF₃), CN ili CO₂H.

4. Spoj ili njegova farmaceutski prihvatljiva sol ili hidrat prema patentnom zahtjevu 1, naznačeno time što prsten A je piridinil izborno supstituiran sa halo ili -C₁-C₄ haloalkil.
5. Spoj ili njegova farmaceutski prihvatljiva sol ili hidrat prema patentnom zahtjevu 1, naznačen time što oba R⁷ i R⁸ su H.
6. Spoj koji ima formulu B, ili njegova farmaceutski prihvatljiva sol ili hidrat naznačen time što:



X je N, CH ili C-halo;

X^a je N ili C-R^{9a}, uz uvjet kada je jedan X^a jednak N, tada su druga dva X^a oba jednaki C-R^{9a};

R⁹ je halo, -C₁-C₄ alkil, -C₁-C₄ haloalkil, -C₁-C₄ hidroksialkil, -NH-S(O)₂-(C₁-C₄ alkil), -S(O)₂NH(C₁-C₄ alkil), -CN, -S(O)₂-(C₁-C₄ alkil), C₁-C₄ alkoksi, -NH(C₁-C₄ alkil), -N(C₁-C₄ alkil)₂, -OH, -OCF₃, -CN, -NH₂, -C(O)NH₂, -C(O)NH(C₁-C₄ alkil), -C(O)-N(C₁-C₄ alkil)₂, -(C₁-C₆ alkilen)-O-(C₁-C₆ alkil), aril i ciklopropil izborno supstituiran sa OH;

svaki R^{9a} je nezavisno izabran od vodika, halo, -C₁-C₄ alkila, -C₁-C₄ haloalkila, -C₁-C₄ hidroksialkila, -NH-S(O)₂-(C₁-C₄ alkil), -S(O)₂NH(C₁-C₄ alkil), -CN, -S(O)₂-(C₁-C₄ alkil), C₁-C₄ alkoksi, -NH(C₁-C₄ alkil), -N(C₁-C₄ alkil)₂, -OH, -OCF₃, -CN, -NH₂, -C(O)NH₂, -C(O)NH(C₁-C₄ alkil), -C(O)-N(C₁-C₄ alkil)₂, -(C₁-C₆ alkilen)-O-(C₁-C₆ alkil), aril i ciklopropila izborno supstituiranog sa OH;

R¹, R³, R⁴ i R⁶ su svaki nezavisno izabrani od vodika, C₁-C₄ alkila, C₁-C₄ haloalkila, -O-C₁-C₄ alkila i CN, pri čemu je svaka navedena alkil grupa od R¹, R³, R⁴ i R⁶ nezavisno izborno supstituirana sa -OH, -NH₂, -CN, -O-C₁-C₄ alkil, -NH(C₁-C₄ alkil) ili -N(C₁-C₄ alkil)₂;

R² i R⁵ su svaki nezavisno izabrani od: -(C₁-C₆ alkil), -(C₁-C₆ alkil)-C(O)-NH₂, -(C₁-C₆ alkil)-CO₂H, -(C₂-C₆ alkenil ili alkinil), -(C₁-C₆ alkilen)-O-(C₁-C₆ alkil), -(C₀-C₆ alkilen)-C(O)N(R⁶)-(C₁-C₆ alkil), -(C₀-C₆ alkilen)-Q, -(C₀-C₆ alkilen)-C(O)-(C₁-C₆ alkil) i -(C₀-C₆ alkilen)-C(O)-(C₀-C₆ alkilen)-Q, gdje:

bilo koja alkil ili alkilen grupa prisutna u R² i R⁵ je izborno supstituirana jednim ili više -OH, -O(C₁-C₄ alkil), -CO₂H ili halo;

bilo koja terminalna metil grupa prisutna u R² i R⁵ je izborno zamijenjena sa -CH₂OH, CF₃, -CH₂F, -CH₂Cl, C(O)CH₃, C(O)CF₃, CN ili CO₂H;

R⁷ i R⁸ su svaki nezavisno izabrani od vodika i C₁-C₆ alkila; i

Q je izabran od arila, heteroarila, karbociklila i heterociklila, od kojih je bilo koji izborno supstituiran; gdje

R¹ i R³ su izborno uzeti zajedno sa atomom ugljika za koji su vezani tako da formiraju C(=O); ili

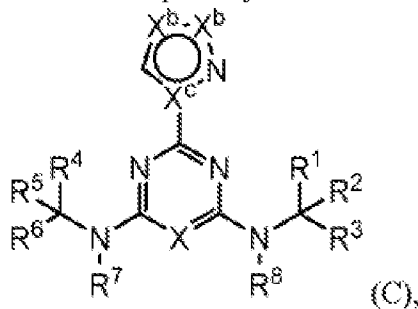
R⁴ i R⁶ su izborno uzeti zajedno sa atomom ugljika za koji su vezani tako da formiraju C(=O); ili

R¹ i R² su izborno uzeti zajedno tako da formiraju izborno supstituiran karbociklil ili izborno supstituiran heterociklil; ili

R⁴ i R⁵ su izborno uzeti zajedno tako da formiraju izborno supstituiran i karbociklil ili izborno supstituiran heterociklil; pri čemu spoj nije izabran iz grupe koju čine:

- (1) 4,6-Pirimidindiamin, 2-(6-metil-2-piridinil)-N⁴,N⁶-dipropil-;
- (2) 4,6-Pirimidindiamin, N⁴-etil-2-(6-metil-2-piridinil)-N⁶-propil-; i
- (3) 4,6-Pirimidindiamin, N⁴,N⁴-dietil-2-(6-metil-2-piridinil)-N⁶-propil-.

7. Spoj koji ima formulu C, ili njegova farmaceutski prihvatljiva sol ili hidrat, naznačen time što:



X je N, CH ili C-halo;

svaki X^b je nezavisno $N-R^{9b}$, O, S, C-H ili $C-R^{9c}$, uz uvjet da najmanje jedan X^b je $C-R^{9c}$, i kada je jedan X^b jednak C-H ili $C-R^{9c}$ i drugi je $C-R^{9c}$ tada je X^c jednak N, i kada je jedan X^b jednak $N-R^{9b}$, O ili S, tada je X^c jednak C;

R^{9b} je vodik ili $-C_1-C_4$ alkil;

R^{9c} je halo, $-C_1-C_4$ alkil, $-C_1-C_4$ haloalkil, $-C_1-C_4$ hidroksialkil, $-NH-S(O)_2-(C_1-C_4)$ alkil, $-S(O)_2NH-(C_1-C_4)$ alkil, $-CN$, $-S(O)_2-(C_1-C_4)$ alkil, C_1-C_4 alkoksi, $-NH-(C_1-C_4)$ alkil, $-N(C_1-C_4)$ alkil₂, $-OH$, $-OCF_3$, $-CN$, $-NH_2$, $-C(O)NH_2$, $-C(O)NH-(C_1-C_4)$ alkil, $-C(O)-N(C_1-C_4)$ alkil₂, $-(C_1-C_6)$ alkilen-O- (C_1-C_6) alkil, aril i ciklopropil izborno supstituiran sa OH; R^1 , R^3 , R^4 i R^6 su svaki nezavisno izabrani od vodika, C_1-C_4 alkila, C_1-C_4 haloalkila, $-O-C_1-C_4$ alkila i CN, pri čemu je svaka navedena alkil grupa od R^1 , R^3 , R^4 i R^6 nezavisno izborno supstituirana sa $-OH$, $-NH_2$, $-CN$, $-O-C_1-C_4$ alkil, $-NH-(C_1-C_4)$ alkil ili $-N(C_1-C_4)$ alkil₂;

R^2 i R^5 su svaki nezavisno izabrani od: $-(C_1-C_6)$ alkil, $-(C_1-C_6)$ alkil-C(O)- NH_2 , $-(C_1-C_6)$ alkil-CO₂H, $-(C_0-C_6)$ alkilen-Q, $-(C_0-C_6)$ alkilen-C(O)- (C_1-C_6) alkil, $-(C_0-C_6)$ alkilen-C(O)- (C_0-C_6) alkilen-Q, gdje:

bilo koja alkil ili alkilen grupa prisutna u R^2 i R^5 je izborno supstituirana sa jednim ili više $-OH$, $-O(C_1-C_4)$ alkil, $-CO_2H$ ili halo;

bilo koja terminalna metil grupa prisutna u R^2 i R^5 je izborno zamijenjena sa $-CH_2OH$, CF_3 , $-CH_2F$, $-CH_2Cl$, $C(O)CH_3$, $C(O)CF_3$, CN ili CO₂H;

R^7 i R^8 su svaki nezavisno izabrani od vodika i C_1-C_6 alkila; i

Q je izabran od arila, heteroarila, karbociklila i heterociklila, od kojih je bilo koji izborno supstituiran; gdje

R^1 i R^3 su izborno uzeti zajedno sa atomom ugljika za koji su vezani tako da formiraju $C(=O)$; ili

R^4 i R^6 su izborno uzeti zajedno sa atomom ugljika za koji su vezani tako da formiraju $C(=O)$; ili

R^1 i R^2 su izborno uzeti zajedno tako da formiraju izborno supstituiran karbociklil ili izborno supstituiran heterociklil; ili

R^4 i R^5 su izborno uzeti zajedno tako da formiraju izborno supstituiran i karbociklil ili izborno supstituiran i heterociklil; gdje:

(i) kada je X jednako CH i



je izborno supstituiran 1-imidazolil, izborno supstituiran i 1-pirolil ili izborno supstituiran i 1-pirazolil, tada ni $N(R^7)C(R^4)(R^5)(R^6)$ ni $N(R^8)C(R^1)(R^2)(R^3)$ nije $NH(CH_2)_7CH_3$, ili $NHCH_2CH_2OH$; i

(ii) kada su X i Xc oba jednaki N, tada ni $N(R^7)C(R^4)(R^5)(R^6)$ ni $N(R^8)C(R^1)(R^2)(R^3)$ nije $N(CH_2CH_3)_2$.

8. Spoj ili njegova farmaceutski prihvatljiva sol ili hidrat prema patentnom zahtjevu 7 naznačeno time što:

a) R^{9c} je halo, $-OH$, CN, $-NH_2$, $-O-C_1-C_4$ alkil, $-NH-(C_1-C_4)$ alkil, $-N(C_1-C_4)$ alkil₂, $-C_1-C_4$ alkil, $-C_1-C_4$ haloalkil i $-(C_1-C_6)$ alkilen-O- (C_1-C_6) alkil);

R^1 i R^4 su svaki vodik;

R^3 i R^6 su svaki nezavisno izabrani od C_1-C_4 alkila, C_1-C_4 haloalkila, $-O-C_1-C_4$ alkila i CN; i

R^2 i R^5 su svaki $-(C_1-C_6)$ alkil, gdje:

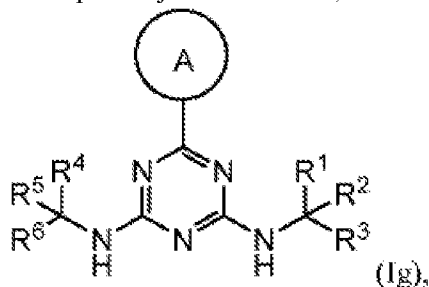
alkil grupa prisutna u R^2 i R^5 je izborno supstituirana sa jednim ili više $-OH$, $-O(C_1-C_4)$ alkil, $-CO_2H$, ili halo; i

bilo koja terminalna metil grupa prisutna u R^2 i R^5 je izborno zamijenjen sa $-CH_2OH$, CF_3 , $-CH_2F$, $-CH_2Cl$, $C(O)CH_3$, $C(O)CF_3$, CN, ili CO₂H; ili

b) R^1 i R^4 su svaki nezavisno izabrani od C_1-C_4 alkila i C_1-C_4 haloalkila, i R^2 i R^5 su svaki $-(C_1-C_6)$ alkil).

9. Spoj ili njegova farmaceutski prihvatljiva sol ili hidrat prema patentnom zahtjevu 1, naznačeno time što R^3 i R^6 su oba vodik, R^1 i R^4 su svaki nezavisno izabrani od C_1-C_4 alkila i C_1-C_4 haloalkila, i R^2 i R^5 su svaki $-(C_1-C_6)$ alkil).

10. Spoj formule (Ig) ili njegova farmaceutski prihvatljiva sol ili hidrat, naznačeno time što:



prsten A je izborno supstituiran 5-6 -člani monocikličan aril ili monocikličan heteroaril;

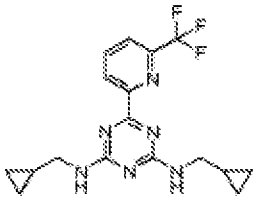
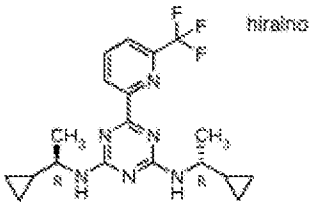
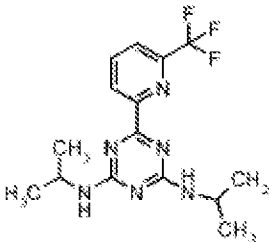
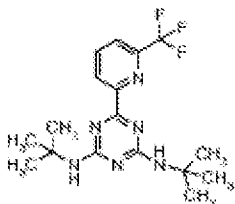
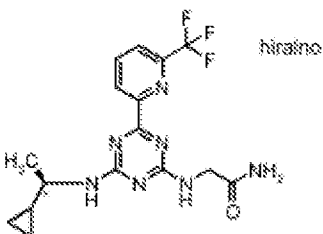
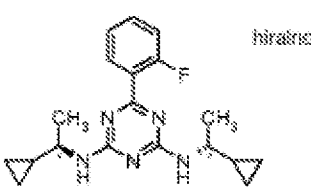
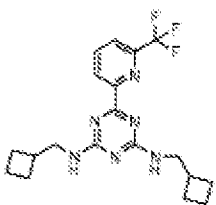
R^3 i R^6 su oba vodik;

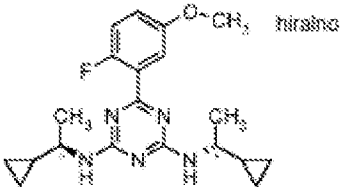
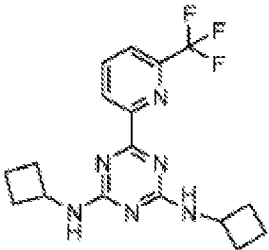
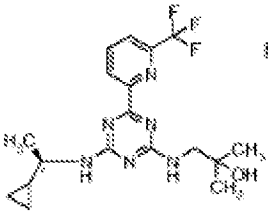
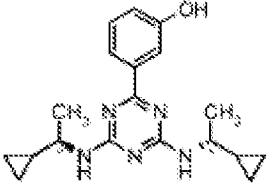
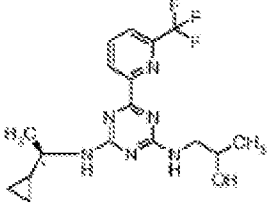
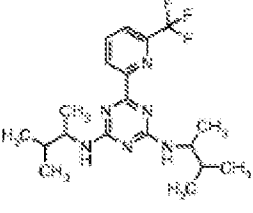
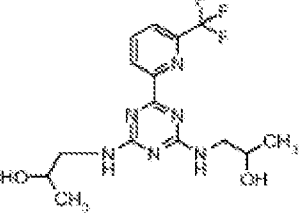
R^1 i R^4 su svaki nezavisno izabrani od C_1-C_4 alkila i C_1-C_4 haloalkila; i

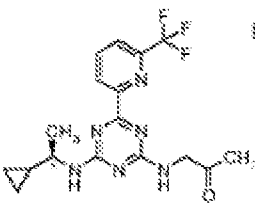
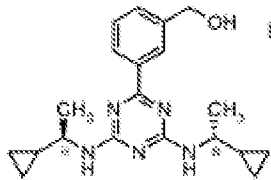
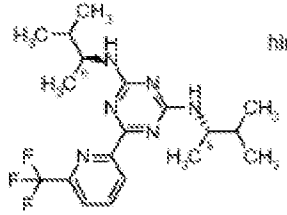
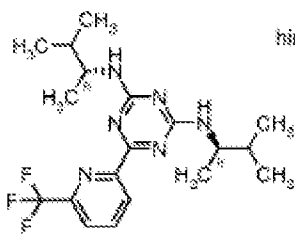
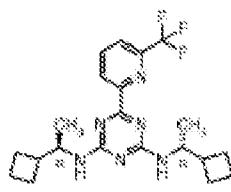
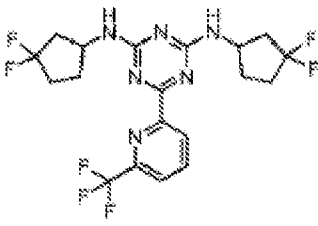
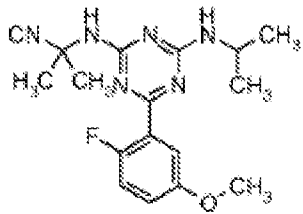
R^2 i R^5 su svaki $-(C_1-C_6)$ alkil; ili

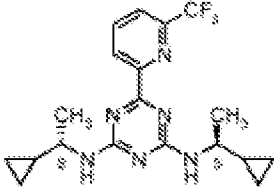
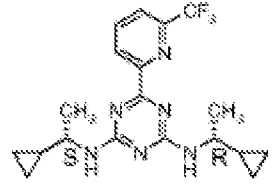
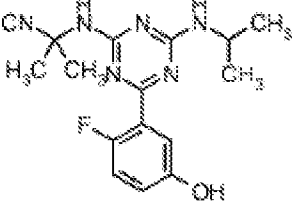
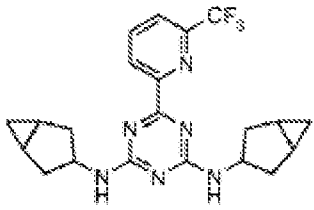
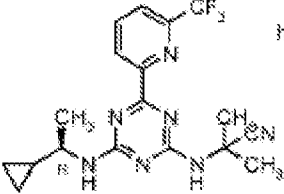
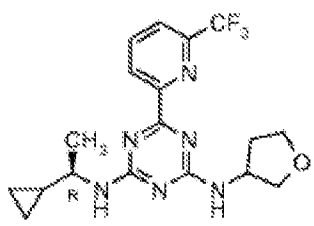
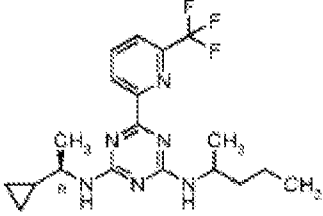
R^1 i R^2 su izbornu uzeti zajedno tako da formiraju izbornu supstituiran i monocikličan karbociklil; ili
 R^4 i R^5 su izbornu uzeti zajedno tako da formiraju izbornu supstituiran monocikličan karbociklil;
gdje:

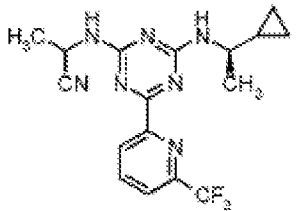
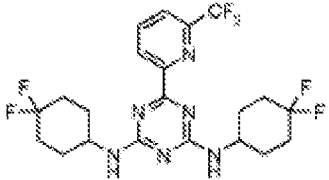
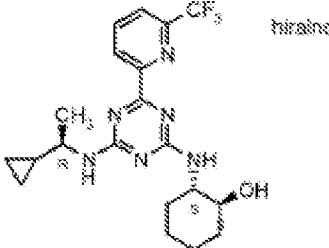
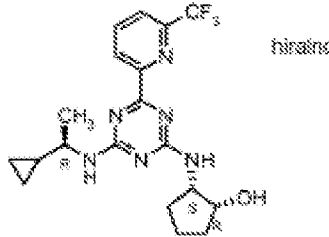
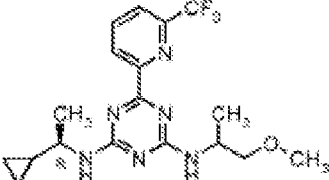
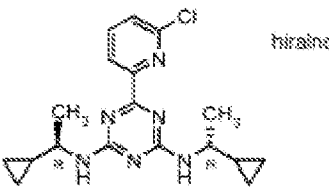
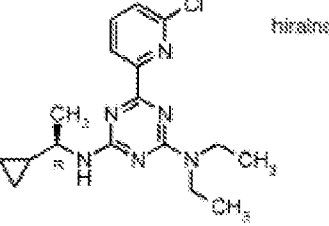
- (i) prsten A nije izbornu supstituiran triazolil, ili 3,5-dimetil-1H-pirazol-1-il,
 - (ii) kada su R^1 i R^2 izbornu uzeti zajedno tako da formiraju nesupstituiran i cikloheksil, i R^4 i R^5 su izbornu uzeti zajedno tako da formiraju nesupstituiran i cikloheksil, tada A nije disupstituiran 1-pirazolil ili nesupstituiran fenil;
 - (iii) spoj nije izabran iz grupe koju čine:
 - (1) 6-(1H-imidazol-1-il)- N^2,N^4 -bis(1-metiletil)-1,3,5-Triazin-2,4-diamin;
 - (2) N^2,N^4 -bis(1-metilpropil)-6-fenil-1,3,5-Triazin-2,4-diamin; ili
 - (3) 1,3,5-triazin-2,4-diamin, 6-(4-hloro-3,5-dimetil-1H-pirazol-1-il)- N^2,N^4 -bis(1-metiletil)-.
11. Spoj prema patentnom zahtjevu 10 ili njegova farmaceutska prihvatljiva sol ili hidrat, naznačen time što A je piridinil izbornu supstituiran sa halo ili $-C_1-C_4$ haloalkilom.
12. Spoj ili njegova farmaceutska prihvatljiva sol ili hidrat, izabran iz grupe koja se sastoji od:

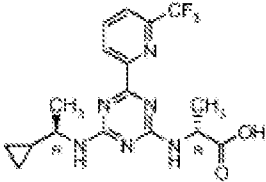
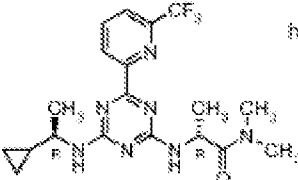
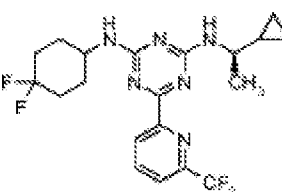
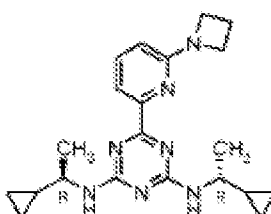
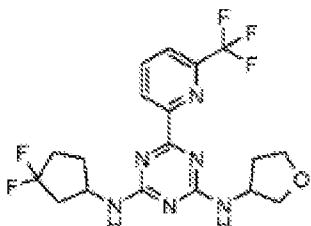
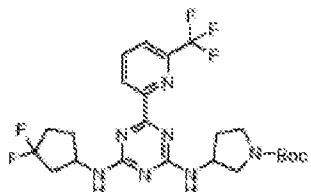
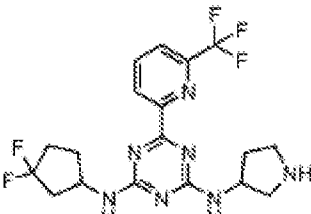
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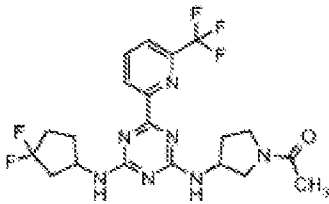
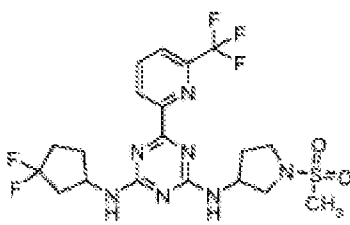
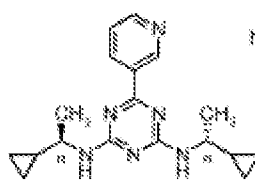
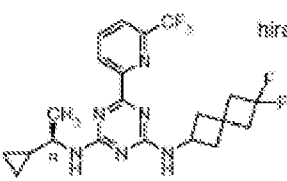
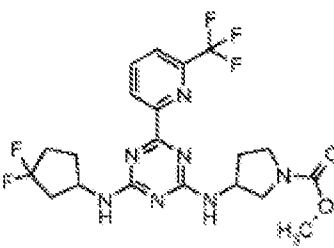
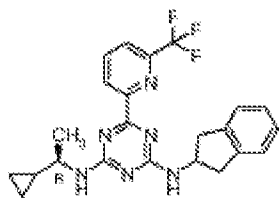
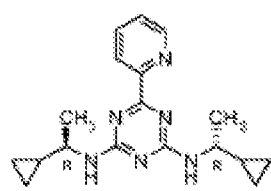
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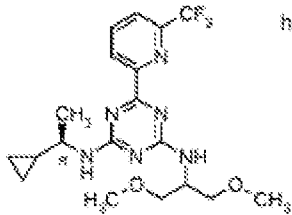
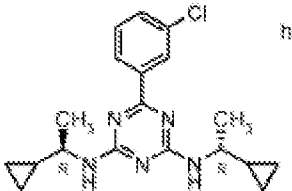
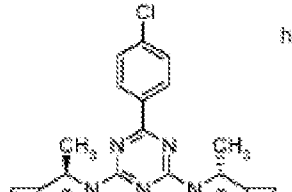
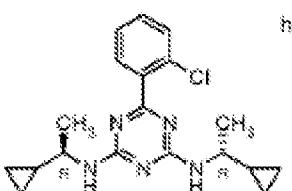
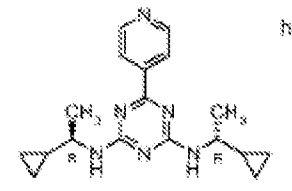
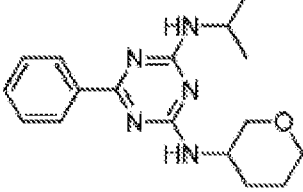
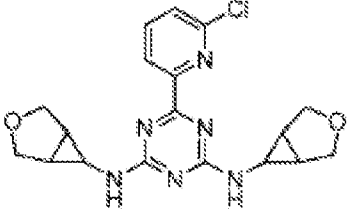
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17	 <chem>CC(C)Nc1nc(NC(C)C)nc2c(NC(C)C)nc(C3=CC=C(C=C3)C(F)(F)F)c2n1</chem> <i>hiralno</i>
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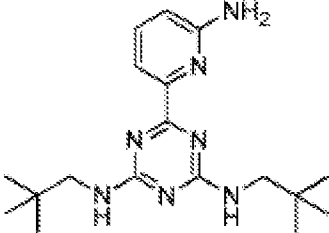
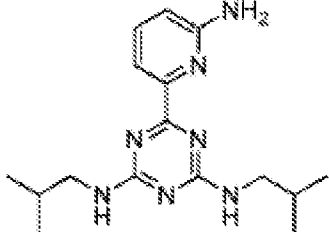
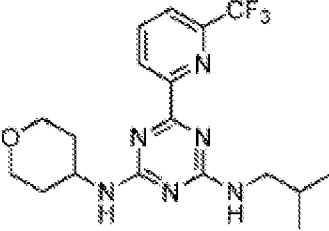
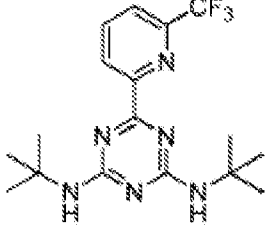
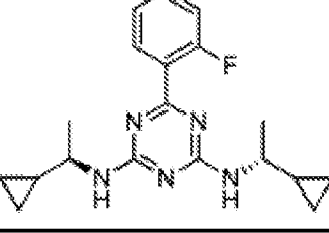
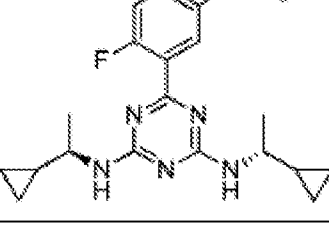
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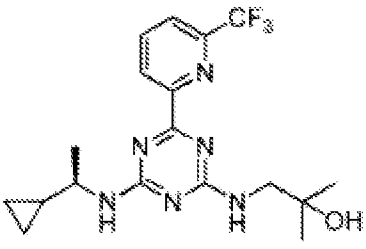
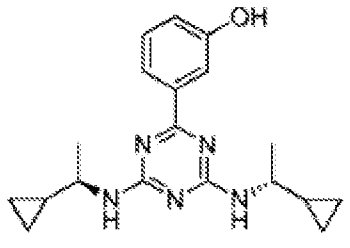
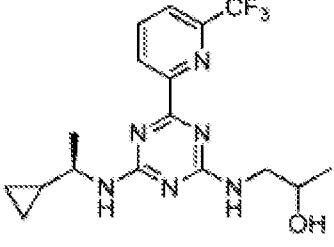
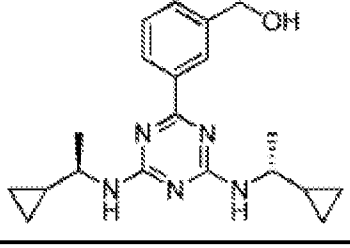
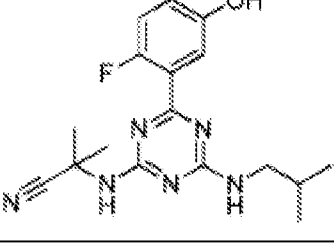
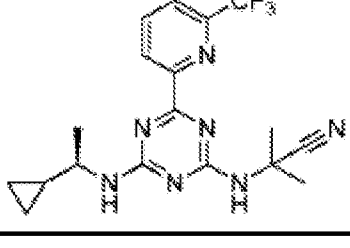
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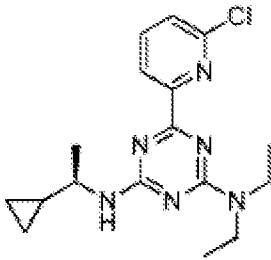
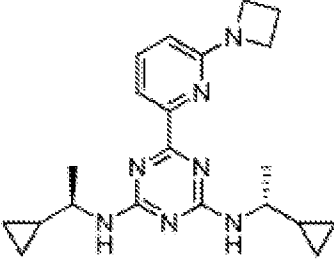
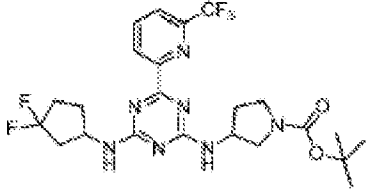
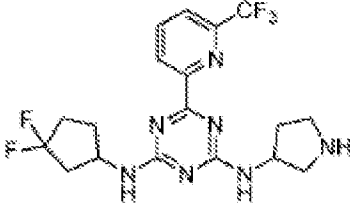
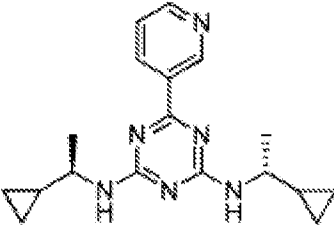
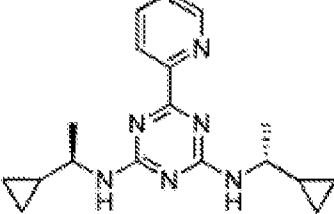
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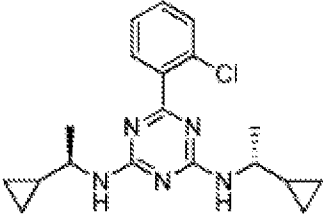
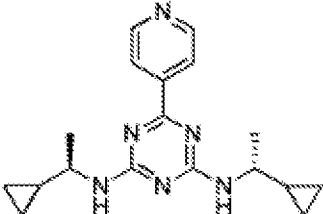
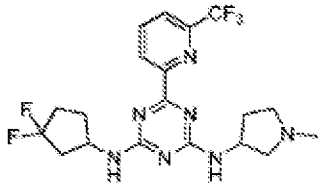
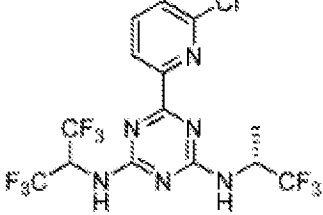
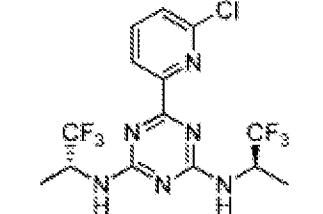
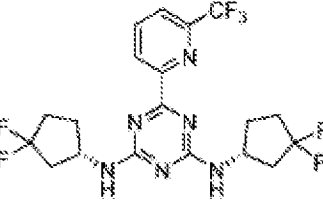
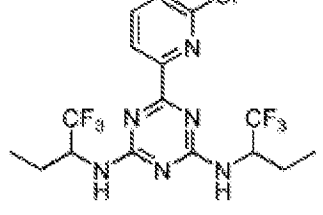
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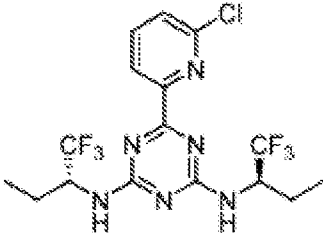
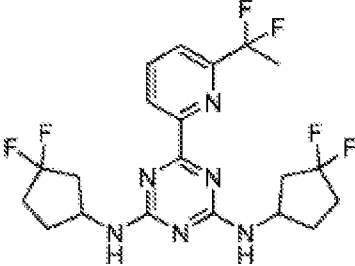
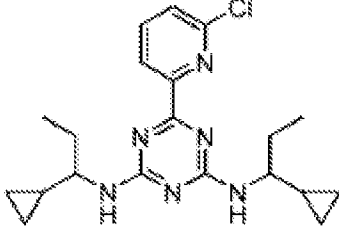
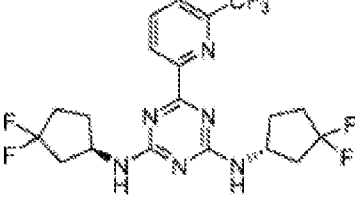
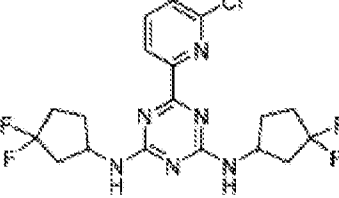
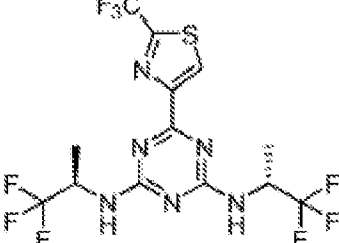
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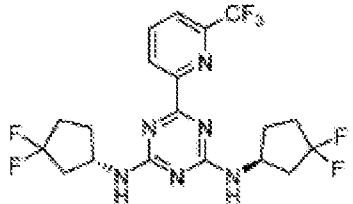
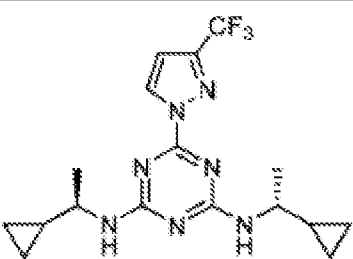
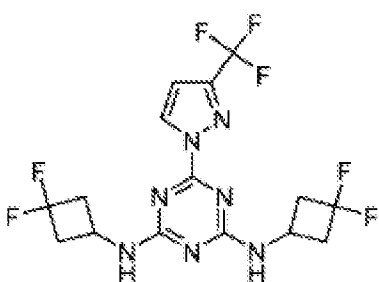
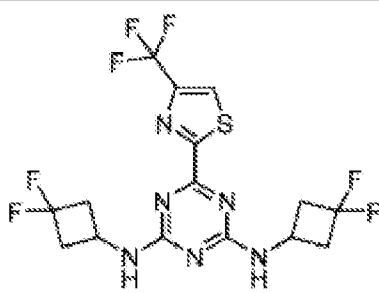
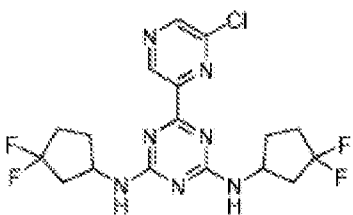
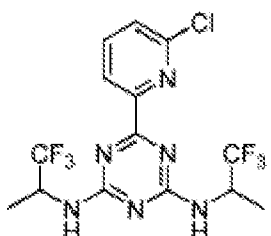
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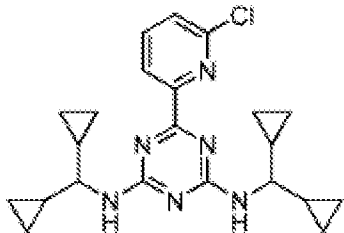
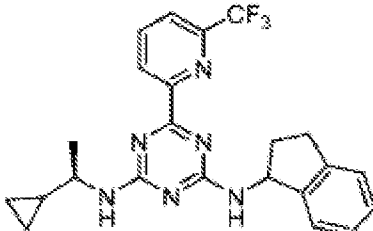
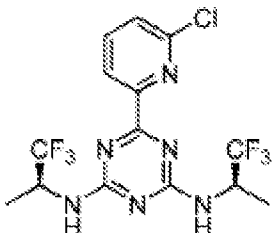
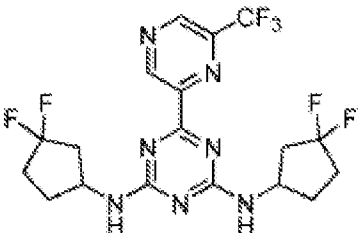
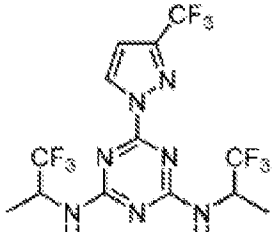
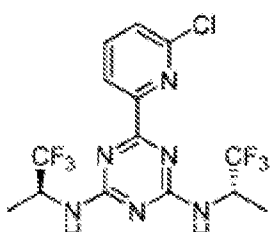
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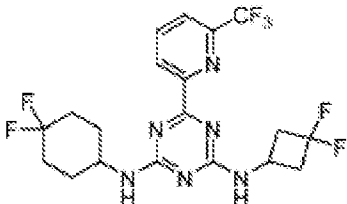
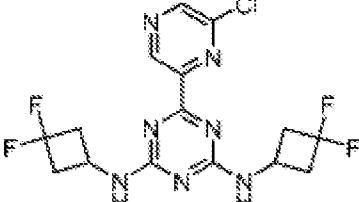
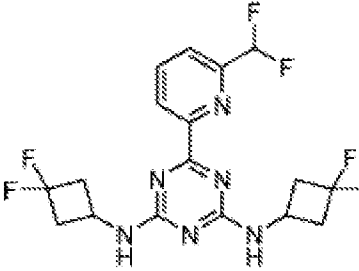
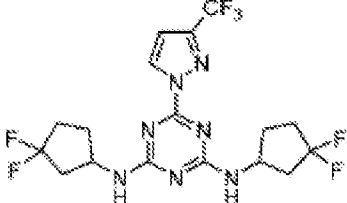
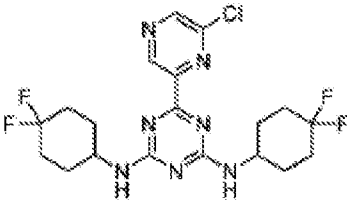
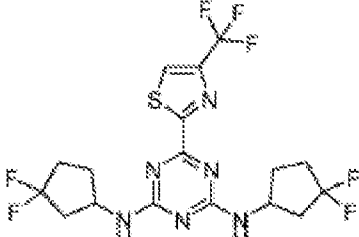
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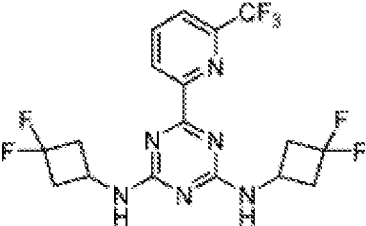
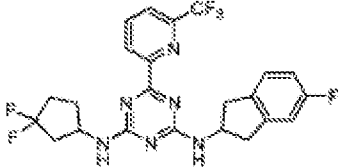
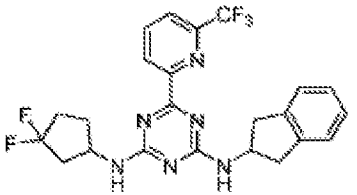
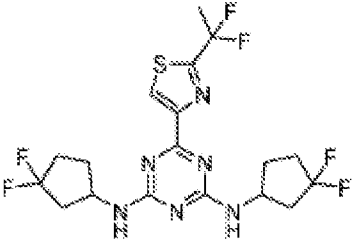
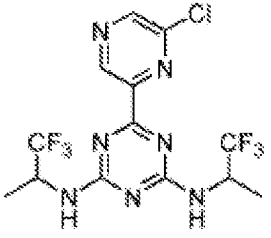
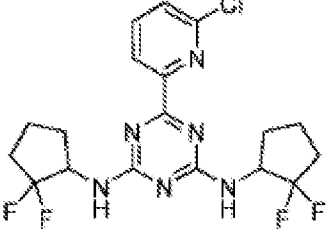
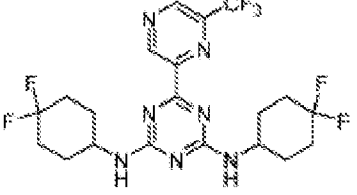
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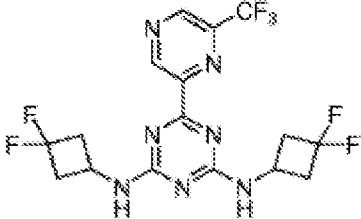
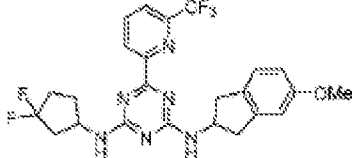
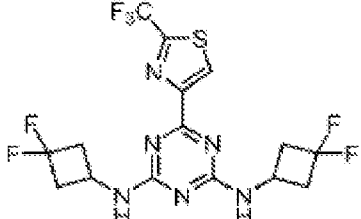
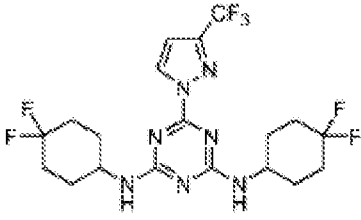
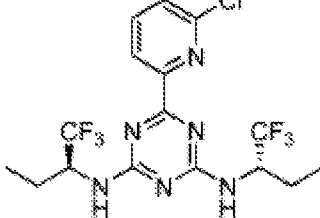
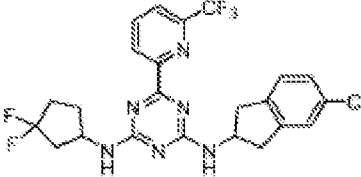
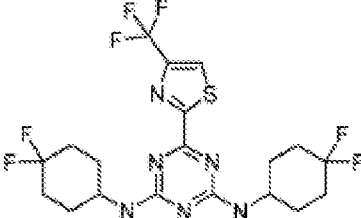
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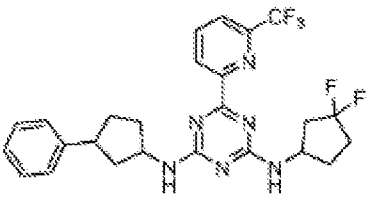
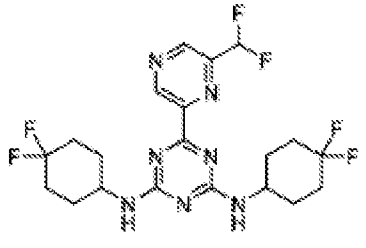
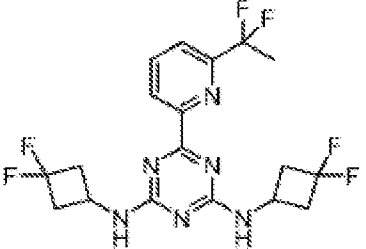
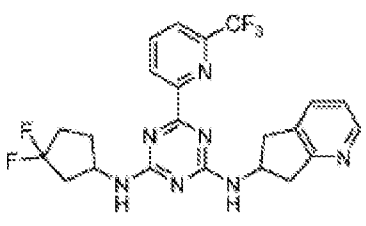
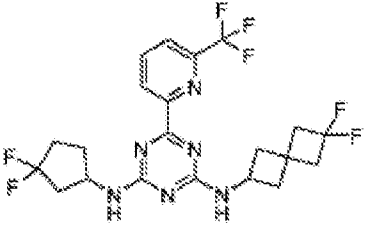
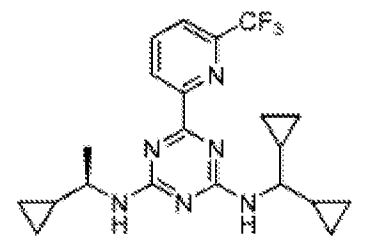
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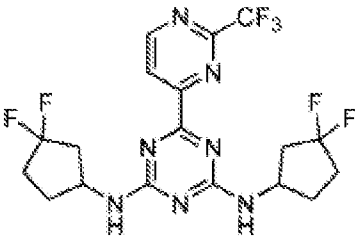
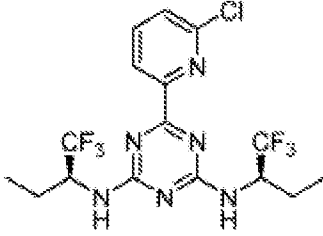
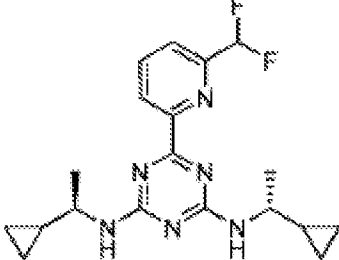
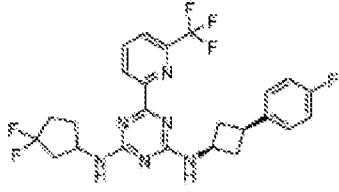
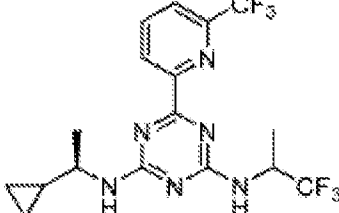
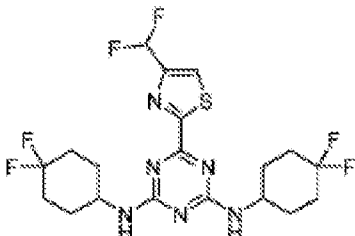
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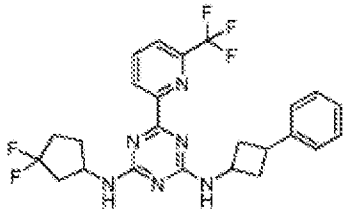
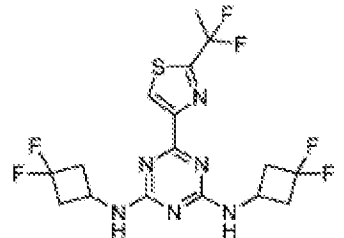
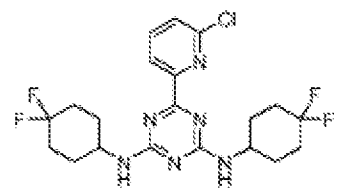
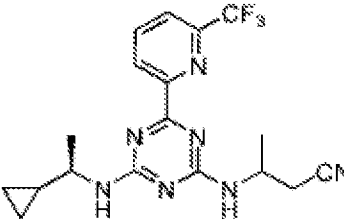
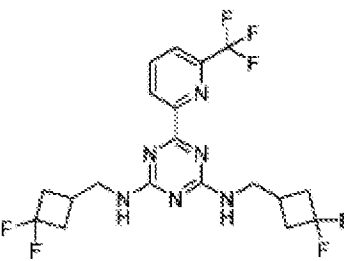
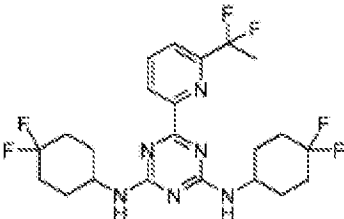
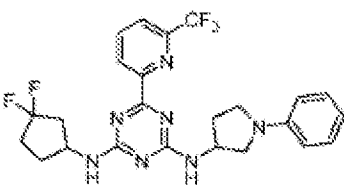
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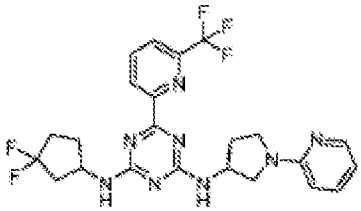
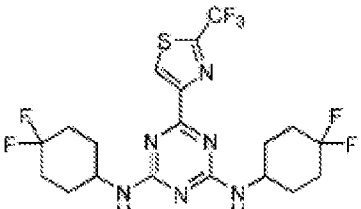
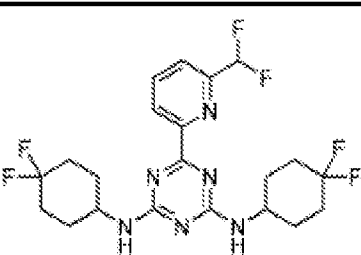
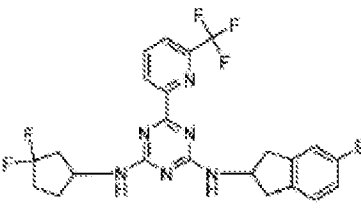
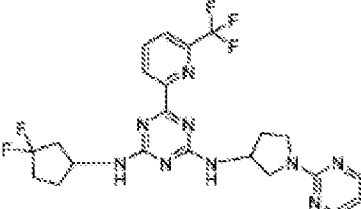
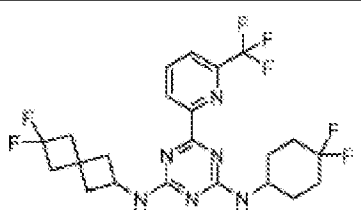
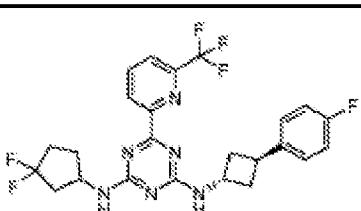
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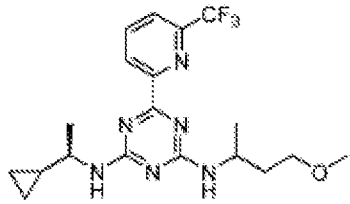
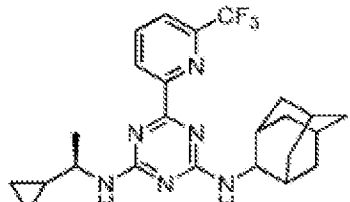
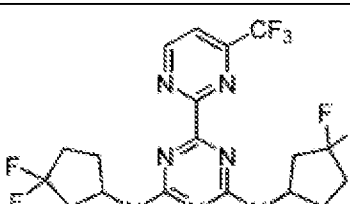
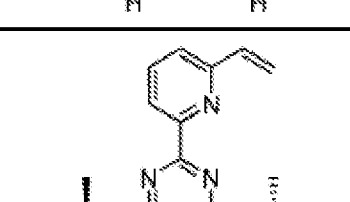
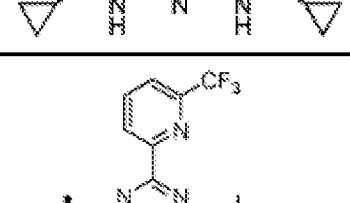
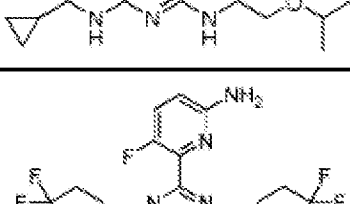
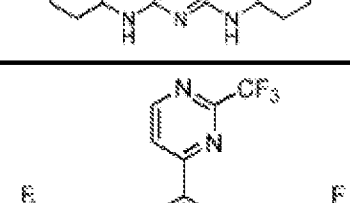
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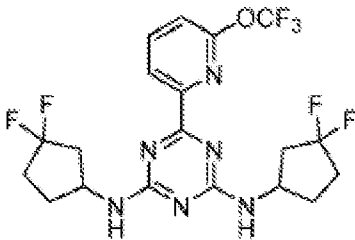
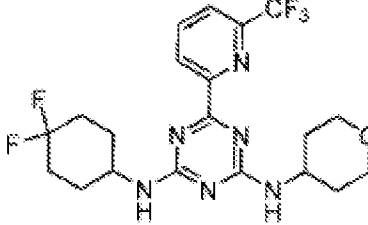
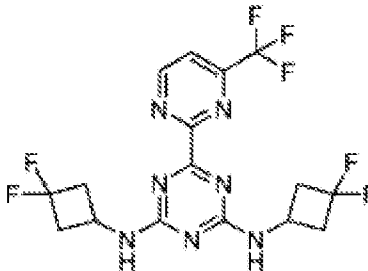
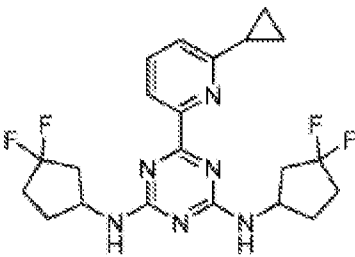
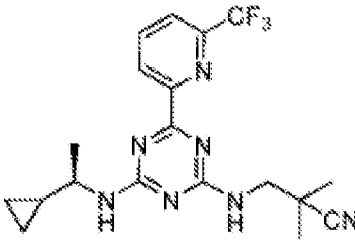
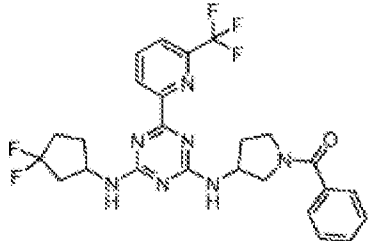
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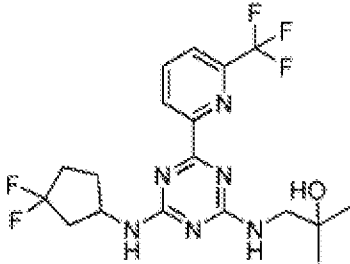
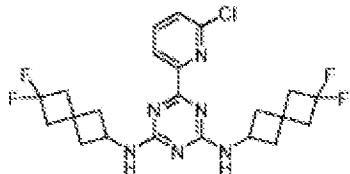
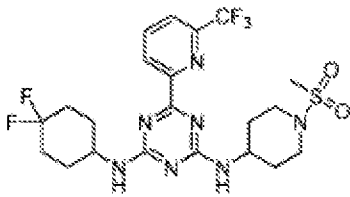
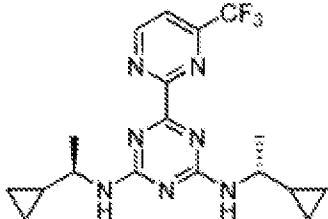
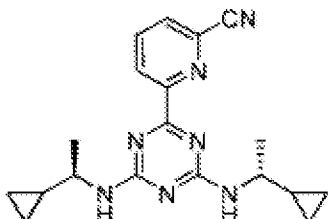
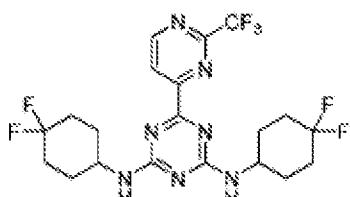
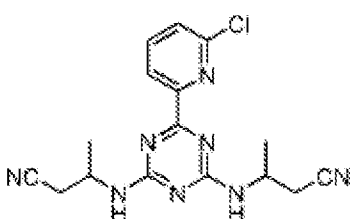
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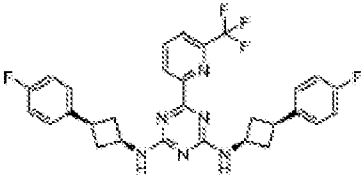
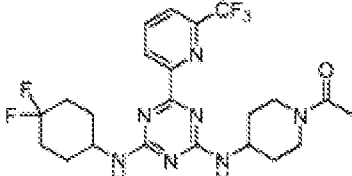
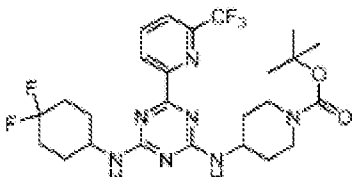
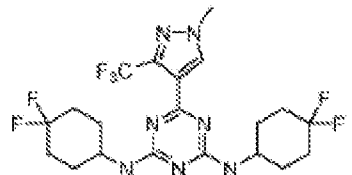
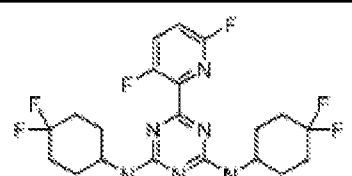
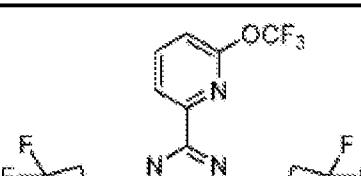
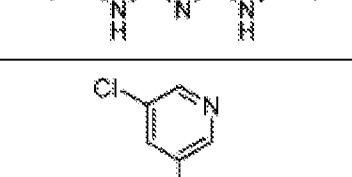
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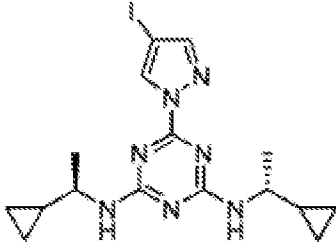
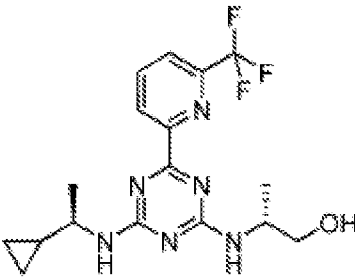
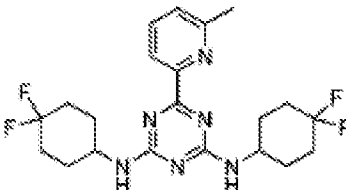
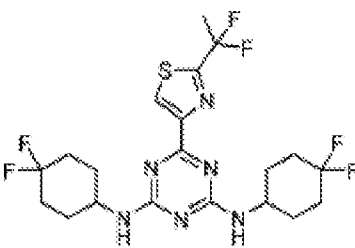
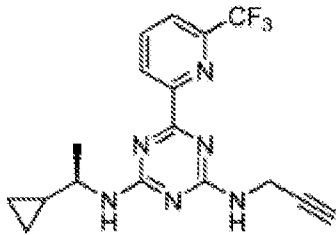
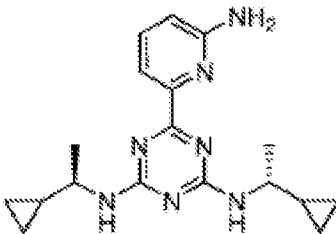
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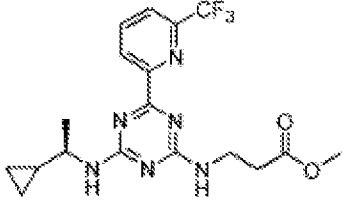
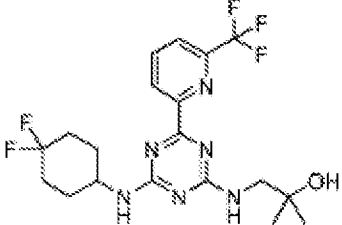
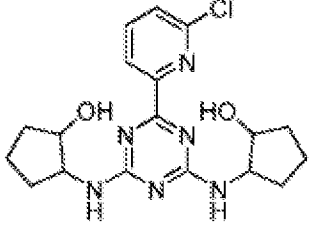
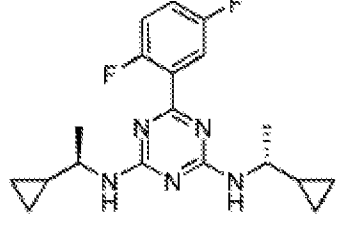
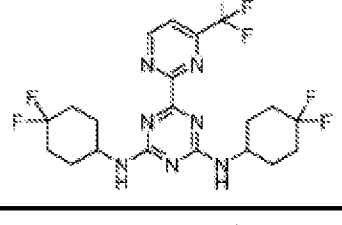
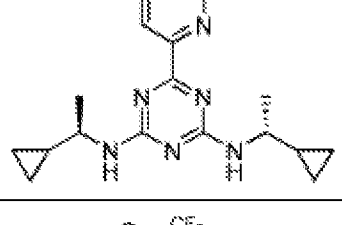
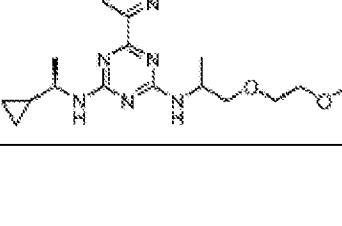
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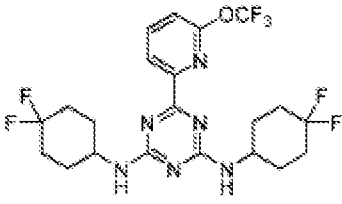
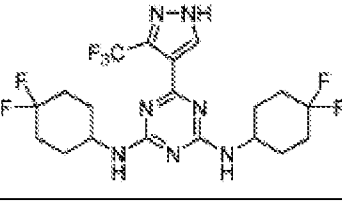
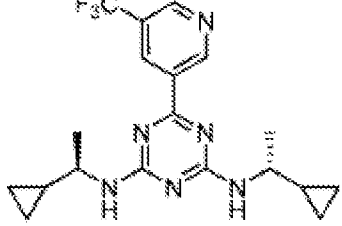
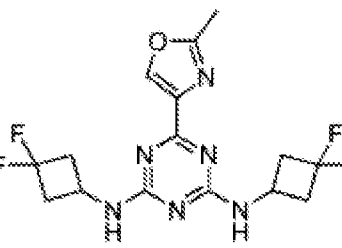
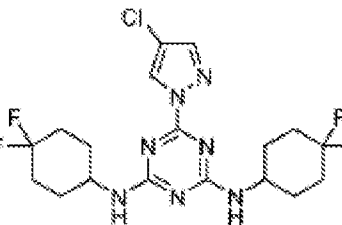
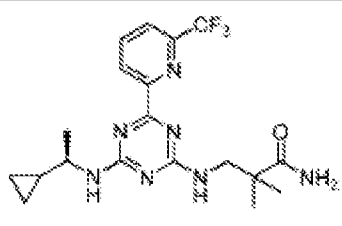
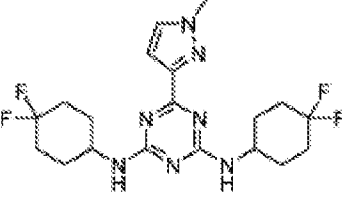
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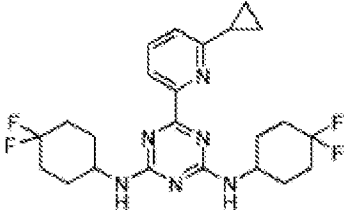
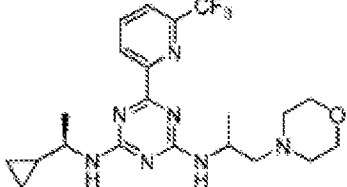
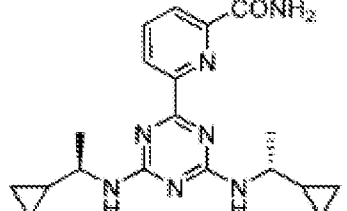
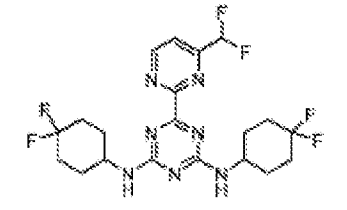
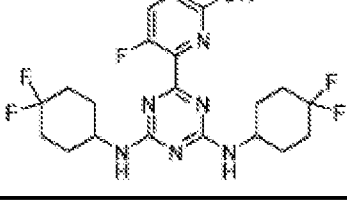
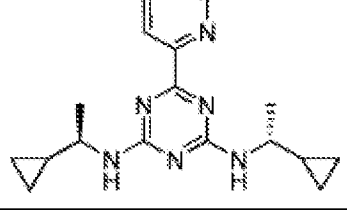
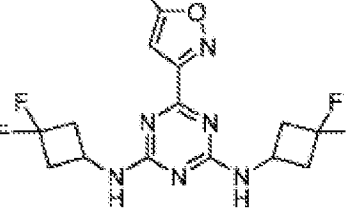
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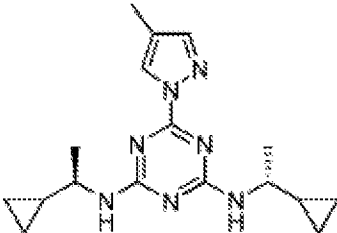
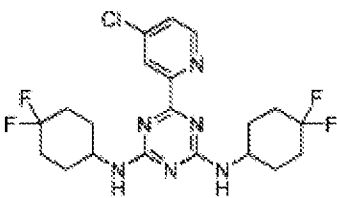
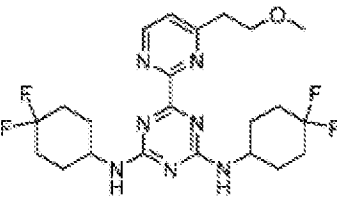
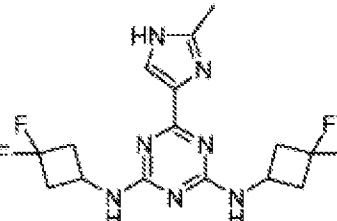
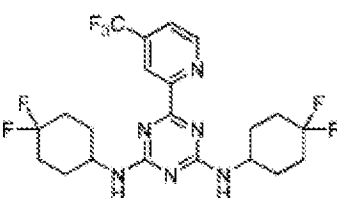
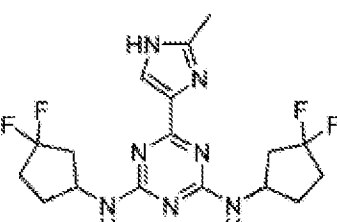
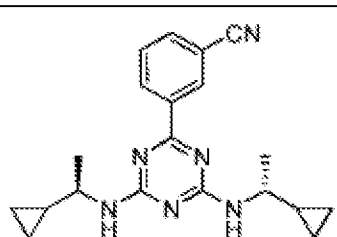
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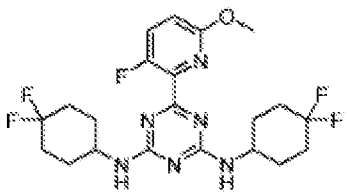
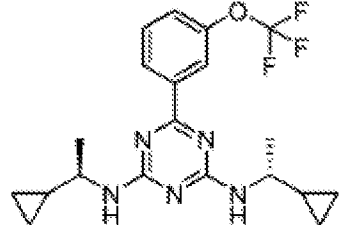
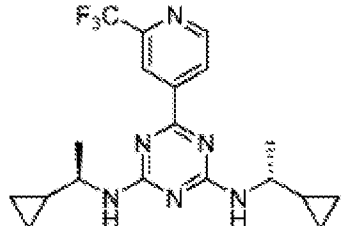
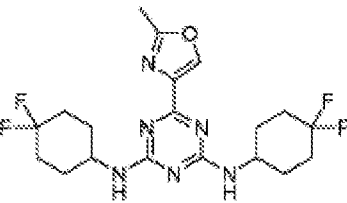
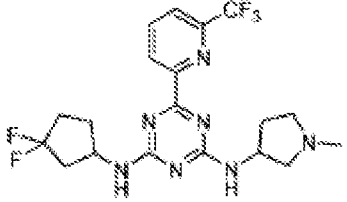
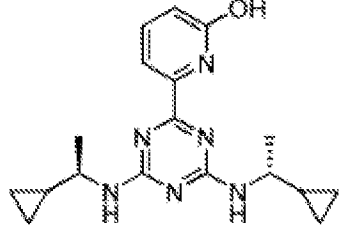
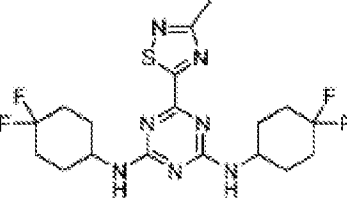
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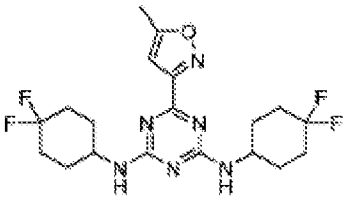
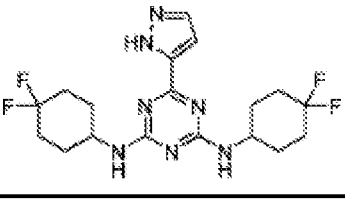
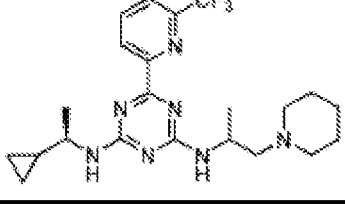
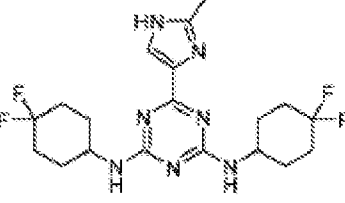
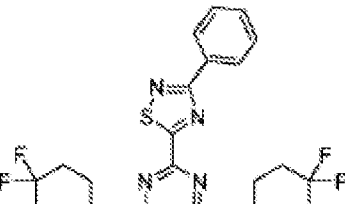
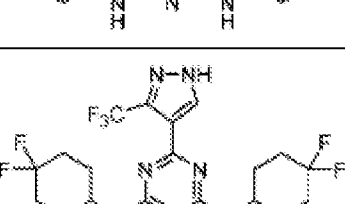
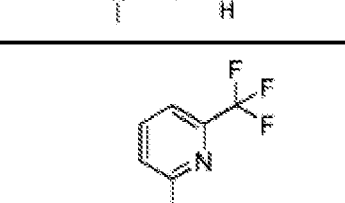
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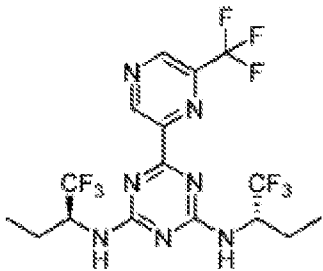
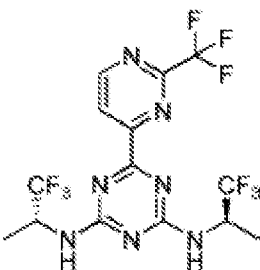
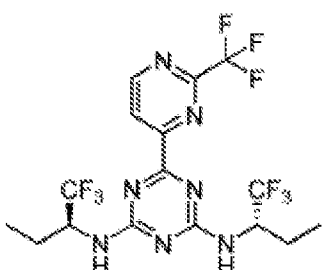
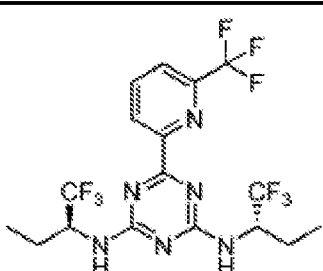
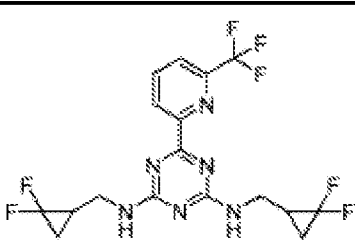
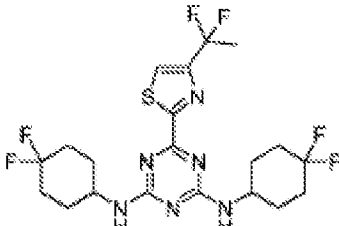
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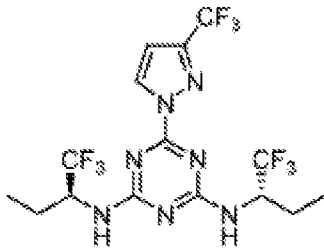
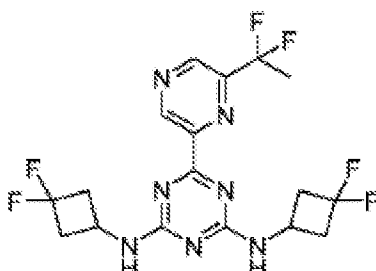
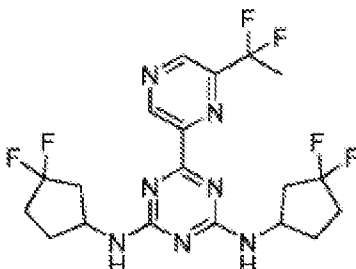
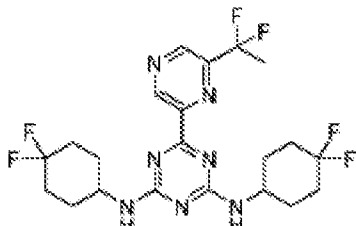
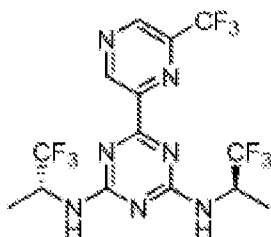
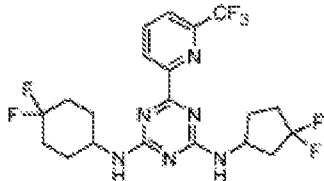
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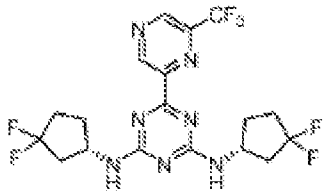
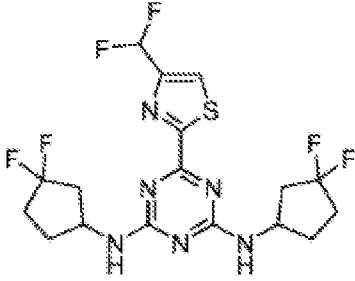
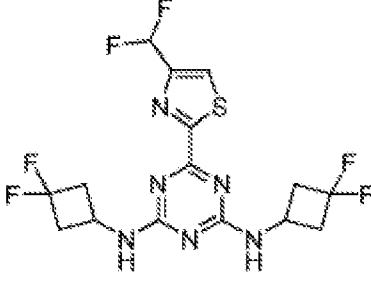
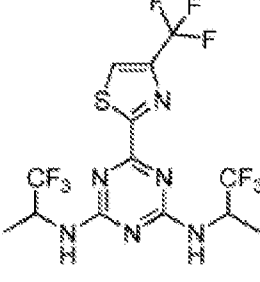
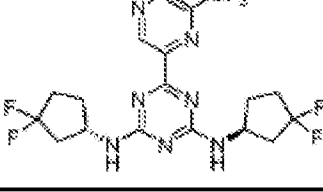
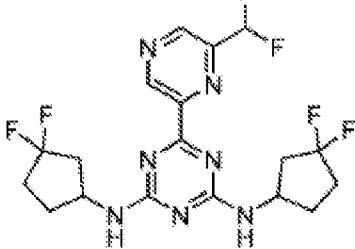
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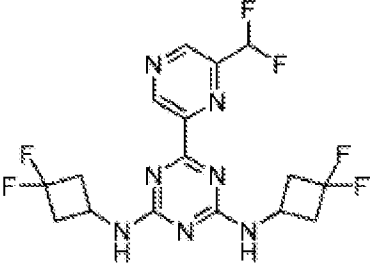
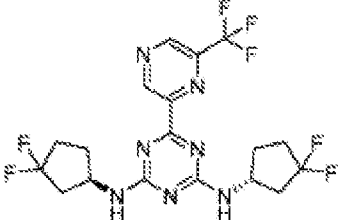
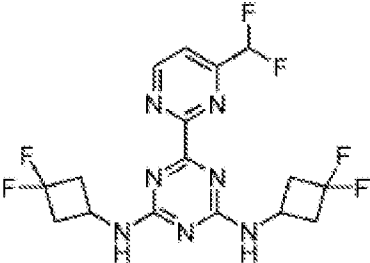
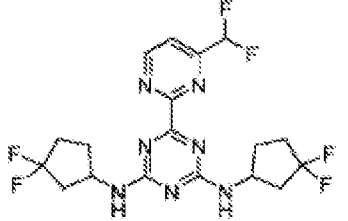
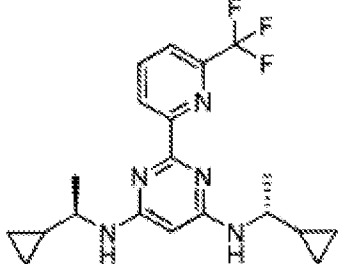
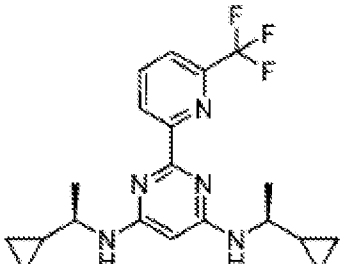
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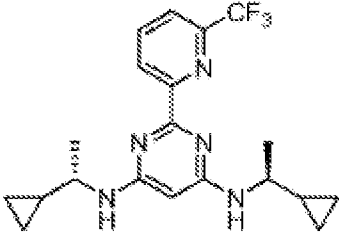
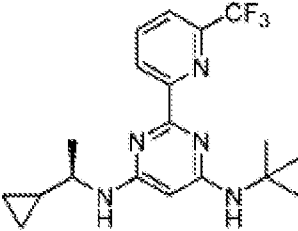
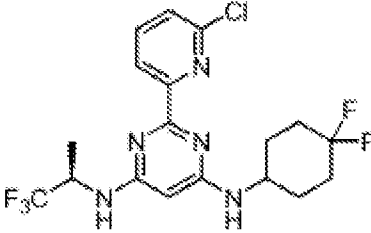
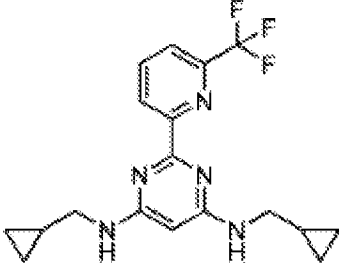
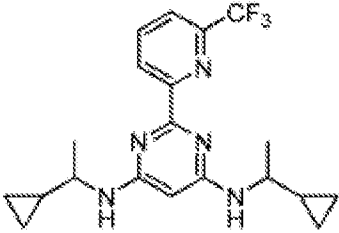
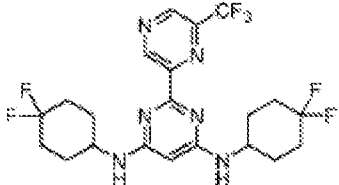
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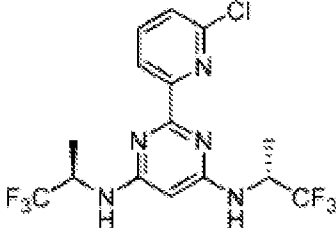
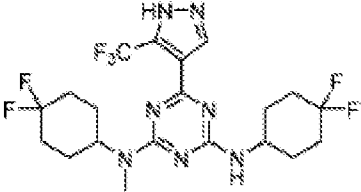
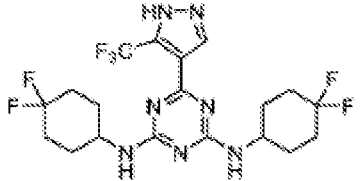
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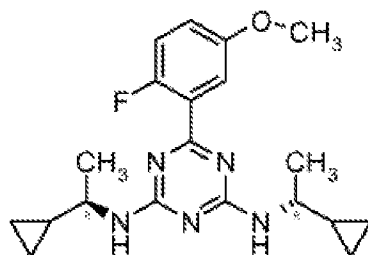
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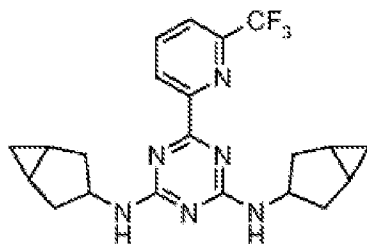
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13. Spoj prema patentnom zahtjevu 12 ili njegova farmaceutski prihvatljiva sol ili hidrat, koji ima strukturu:

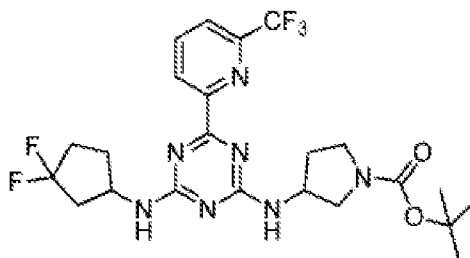


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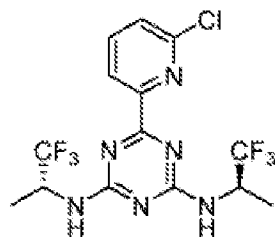


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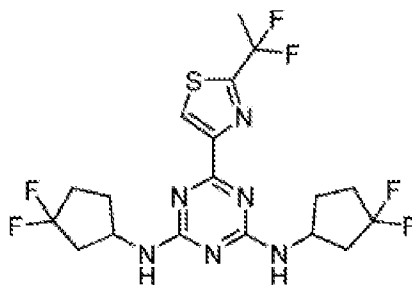
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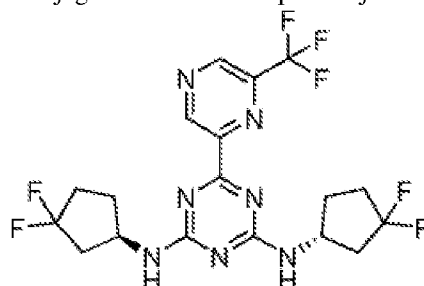
16. Spoj prema patentnom zahtjevu 12 ili njegova farmaceutski prihvatljiva sol ili hidrat, koji ima strukturu:



17. Spoj prema patentnom zahtjevu 12 ili njegova farmaceutski prihvatljiva sol ili hidrat, koji ima strukturu:

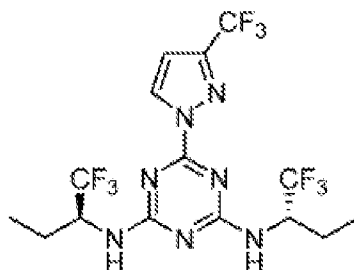


18. Spoj prema patentnom zahtjevu 12 ili njegova farmaceutski prihvatljiva sol ili hidrat, koji ima strukturu:

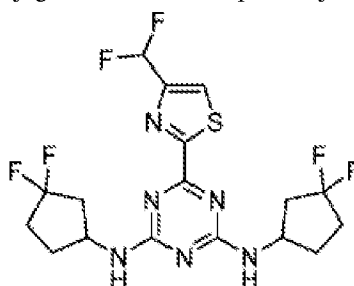


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19. Spoj prema patentnom zahtjevu 12 ili njegova farmaceutski prihvatljiva sol ili hidrat, koji ima strukturu:

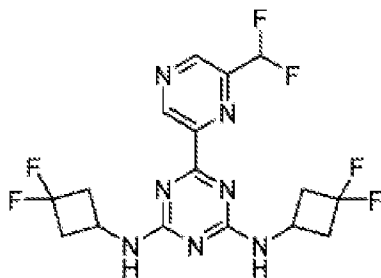


20. Spoj prema patentnom zahtjevu 12 ili njegova farmaceutski prihvatljiva sol ili hidrat, koji ima strukturu:

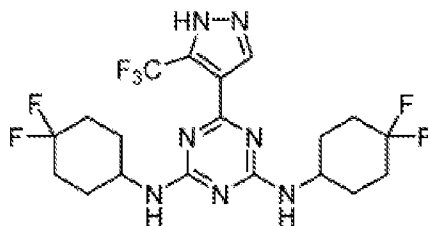


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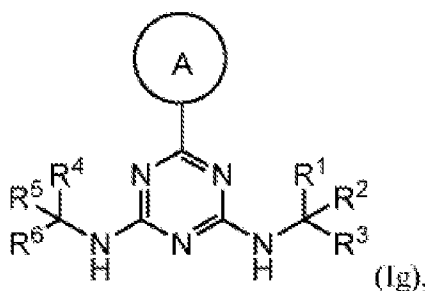
21. Spoj prema patentnom zahtjevu 12 ili njegova farmaceutski prihvatljiva sol ili hidrat, koji ima strukturu:



22. Spoj prema patentnom zahtjevu 12 ili njegova farmaceutski prihvatljiva sol ili hidrat, koji ima strukturu:



23. Farmaceutska kompozicija koja sadrži spoj ili njegovu farmaceutski prihvatljivu sol ili hidrat prema bilo kojem od patentnih zahtjeva 1 do 9 ili 11 do 22, i farmaceutski prihvatljiv nosač.
24. Farmaceutska kompozicija koja sadrži spoj koji ima formulu Ig ili njegovu farmaceutski prihvatljivu sol ili hidrat:



gdje

prsten A je izorno supstituiran 5-6 člani monocikličan aril ili monocikličan heteroaril;

R^3 i R^6 su oba vodik ;

R^1 i R^4 su svaki nezavisno izabrani od C_1 - C_4 alkila i C_1 - C_4 haloalkila; i

R^2 i R^5 su svaki -(C_1 - C_6 alkil); ili

R^1 i R^2 su izorno uzeti zajedno tako da formiraju izorno supstituiran monocikličan karbociklil; ili

R^4 i R^5 su izorno uzeti zajedno tako da formiraju izorno supstituiran monocikličan karbociklil;

gdje:

(i) prsten A nije izorno supstituiran triazolil ili 3,5-dimetil-1H-pirazol-1-il,

(ii) kada su R^1 i R^2 izorno uzeti zajedno tako da formiraju nesupstituiran i cikloheksil, i R^4 i R^5 su izorno uzeti zajedno tako da formiraju nesupstituiran i cikloheksil, tada A nije disupstituiran i 1-pirazolil ili nesupstituiran i fenil;

(iii) spoj nije izbran iz grupe koju čine:

(1) 6-(1H-imidazol-1-il)- N^2 , N^4 -bis(1-metiletil)-1,3,5-Triazin-2,4-diamin; ili

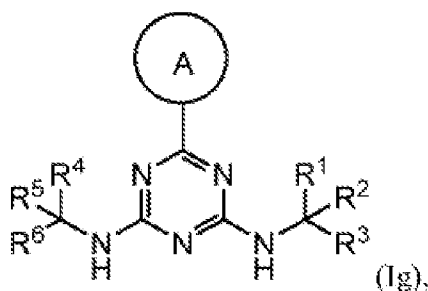
(2) N^2 , N^4 -bis(1-metilpropil)-6-fenil-1,3,5-Triazin-2,4-diamin;

i farmaceutski prihvatljiv nosač.

25. Farmaceutska kompozicija prema bilo kojem od patentnih zahtjeva 23 do 24, naznačena time što dodatno sadrži drugo terapijsko sredstvo korisno u liječenju karcinoma.

26. Spoj, ili njegova farmaceutski prihvatljiva sol ili hidrat, ili farmaceutska kompozicija prema bilo kojem od patentnih zahtjeva 1 do 9 ili 11 do 25 za upotrebu u postupku za liječenje karcinoma **naznačeno** prisustvom IDH1 mutacije, pri čemu IDH1 mutacija rezultira u novoj sposobnosti enzima da katalizira NADPH-zavisnu redukciju α -ketoglutarata u R (-)-2-hidroksiglutarat u pacijentu.

27. Spoj koji ima formulu Ig ili njegova farmaceutski prihvatljiva sol ili hidrat:



gdje

prsten A je izborno supstituiran 5-6 –člani monociklični aril ili monociklični heteroaril;

R³ i R⁶ su oba vodik ;

R¹ i R⁴ su svaki nezavisno izabrani od C₁-C₄ alkila i C₁-C₄ haloalkila; i

R² i R⁵ su svaki -(C₁-C₆ alkil); ili

R¹ i R² su izborno uzeti zajedno tako da formiraju izborno supstituiran monocikličan karbociklil; ili

R⁴ i R⁵ su izborno uzeti zajedno tako da formiraju izborno supstituiran monocikličan karbociklil;

gdje:

(i) prsten A nije izborno supstituiran triazolil, ili 3,5-dimetil-1H-pirazol-1-il,

(ii) kada su R¹ i R² izborno uzeti zajedno tako da formiraju nesupstituiran i cikloheksil, i R⁴ i R⁵ su izborno uzeti zajedno tako da formiraju nesupstituiran i cikloheksil, tada A nije disupstituiran 1-pirazolil ili nesupstituiran fenil;

(iii) spoj nije izabran iz grupe koju čine:

(1) 6-(1H-imidazol-1-il)-N²,N⁴-bis(1-metiletil)-1,3,5-Triazin-2,4-diamin; ili

(2) N²,N⁴-bis(1-metilpropil)-6-fenil-1,3,5-Triazin-2,4-diamin;

za upotrebu u postupku za liječenje karcinoma **naznačeno** prisustvom IDH1 mutacije, gdje IDH1 mutacija rezultira u novoj sposobnosti enzima da katalizira NADPH-zavisnu redukciju α-ketoglutarata u R(-)-2-hidroksiglutarat u pacijenta.

28. Spoj ili njegova farmaceutska prihvatljiva sol ili hidrat, ili farmaceutska kompozicija za upotrebu prema bilo kojem od patentnih zahtjeva 26 do 27, pri čemu IDH1 mutacija je IDH1 R132H ili R132C mutacija; i/ili pri čemu je karcinom izabran od glioma (glioblastoma), akutne mijelogene leukemije, sarkoma, melanoma, nesitnostaničnog karcinoma pluća (NSCLC), holangiokarcinoma, hondrosarkoma, mijelodisplastičnih sindroma (MDS), mijeloproliferativne neoplazme (MPN), karcinoma debelog crijeva ili angio-imunoblastičnog ne-Hodgkin-ovog limfoma (NHL) kod pacijenta, pri čemu, poželjno, karcinom je gliom.