

q is 1, 2, or 3;

r is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

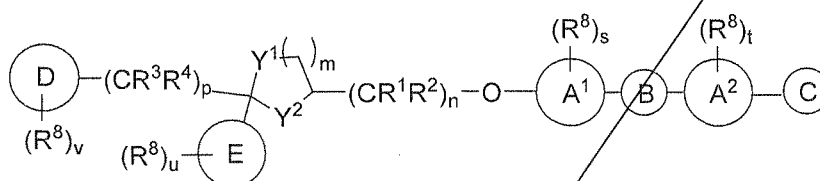
s is 0, 1, 2, 3, or 4;

t is 0, 1, 2, 3, or 4;

u is 0, 1, 2, 3, 4 or 5; and

v is 0, 1, 2, 3, or 4.

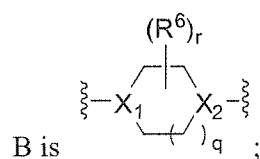
[0004a] In another aspect, there is provided the use of a therapeutically effective amount of a compound of Formula (I), a pharmaceutically acceptable salt, solvate, polymorph, prodrug, metabolite, N-oxide, stereoisomer, or isomer thereof:



Formula (I)

wherein:

A¹ and A² are independently selected from aryl or heteroaryl;



B is

C is optionally substituted 5- or 6-membered heterocyclyl or optionally substituted 5- or 6-membered heteroaryl, wherein the heterocyclyl or the heteroaryl contains 1 to 4 nitrogen atoms;

D is aryl or heteroaryl;

E is aryl, heteroaryl, carbocyclyl, heterocyclyl, or alkyl;

each R¹, R², R³, and R⁴ is independently selected from H, alkyl, haloalkyl, or alkoxy;

X₁ and X₂ are independently selected from N and CR⁵;

R⁵ is H, OH, alkyl, or alkoxy;

each R⁶ is independently alkyl, haloalkyl, halo, alkoxy, -alkylene(NR¹³R¹⁴), or aryl;

each R⁸ is independently selected from alkyl, cycloalkyl, heterocyclyl, halo, hydroxy, nitrile, azido, nitro, alkoxy, haloalkoxy, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene(NR¹³R¹⁴), -alkylene(cycloalkyl), -alkylene(heterocyclyl), aryl, heteroaryl, -SR¹³, -SOR¹³, -SO₂R¹³, -SO₂NR¹³R¹⁴, -NR¹³R¹⁴, -NR¹³SO₂R¹⁴, -NR¹³C(O)R¹⁴, -NR¹³C(O)OR¹⁴, -NR¹³C(O)NR¹³R¹⁴, -C(O)R¹⁴, -C(O)OR¹⁴, and -C(O)NR¹³R¹⁴; or two adjacent R⁸ form a heterocyclyl ring;

each R¹³ and R¹⁴ is independently selected from H, alkyl, cycloalkyl, heterocyclylalkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, arylalkyl, heteroarylalkyl, aryl,

and heteroaryl; or R^{13} and R^{14} taken together form a heterocycle with the atoms to which they are attached;

Y^1 and Y^2 are independently selected from O, CH_2 , NH, and NR^{13} ;

n is 1, 2, or 3;

m is 1 or 2;

p is 1, 2, 3, or 4;

q is 1, 2, or 3;

r is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

s is 0, 1, 2, 3, or 4;

t is 0, 1, 2, 3, or 4;

u is 0, 1, 2, 3, 4 or 5; and

v is 0, 1, 2, 3, or 4, in the manufacture of a medicament for treating fibrosis, a disorder characterized by fibrosis, or a disease characterized by fibrosis.

[0005] In some embodiments described above or below of a compound of Formula (I), X_1 and X_2 are N

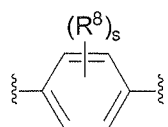
[0006] In some embodiments described above or below of a compound of Formula (I), X_1 is CR^5 and X_2 is N.

[0007] In some embodiments described above or below of a compound of Formula (I), X_1 is N and X_2 is CR^5 .

[0008] In some embodiments described above or below of a compound of Formula (I), q is 1 and r is 0.

[0009] In some embodiments described above or below of a compound of Formula (I), A^1 is aryl.

[0010] In some embodiments described above or below of a compound of Formula (I), A^1 is



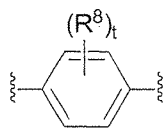
[0011] In some embodiments described above or below of a compound of Formula (I), A^1 is



[0012] In some embodiments described above or below of a compound of Formula (I), A^1 is heteroaryl.

[0013] In some embodiments described above or below of a compound of Formula (I), A^2 is aryl.

[0014] In some embodiments described above or below of a compound of Formula (I), A² is



[0015] In some embodiments described above or below of a compound of Formula (I), A² is



[0016] In some embodiments described above or below of a compound of Formula (I), A² is heteroaryl.

q is 1, 2, or 3;

r is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

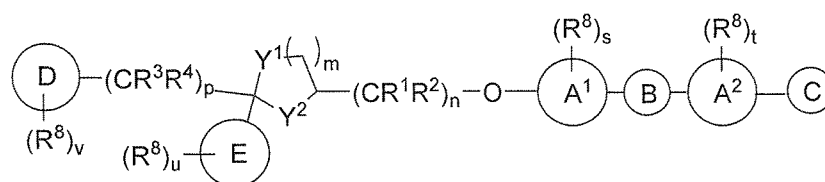
s is 0, 1, 2, 3, or 4;

t is 0, 1, 2, 3, or 4;

u is 0, 1, 2, 3, 4 or 5; and

v is 0, 1, 2, 3, or 4.

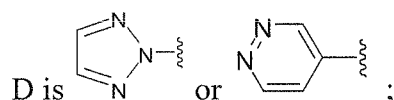
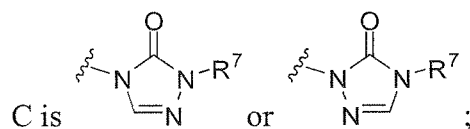
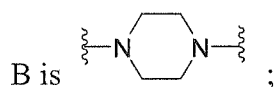
[0004a] In another aspect, there is provided the use of a therapeutically effective amount of a compound of Formula (I), a pharmaceutically acceptable salt, solvate, stereoisomer, or isomer thereof:



Formula (I)

wherein:

A¹ and A² are independently selected from aryl or heteroaryl;



E is aryl, heteroaryl, carbocyclyl, or heterocyclyl;

each R¹, R², R³, and R⁴ is H;

R⁷ is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene(NR¹³R¹⁴), cycloalkyl, heterocyclyl, -alkylene(cycloalkyl), or -alkylene(heterocyclyl);

each R⁸ is independently selected from alkyl, cycloalkyl, heterocyclyl, halo, hydroxy, nitrile, azido, nitro, alkoxy, haloalkoxy, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene(NR¹³R¹⁴), -alkylene(cycloalkyl), -alkylene(heterocyclyl), aryl, heteroaryl, -SR¹³, -SOR¹³, -SO₂R¹³, -SO₂NR¹³R¹⁴, -NR¹³R¹⁴, -NR¹³SO₂R¹⁴, -NR¹³C(O)R¹⁴, -NR¹³C(O)OR¹⁴, -NR¹³C(O)NR¹³R¹⁴, -C(O)R¹⁴, -C(O)OR¹⁴, and -C(O)NR¹³R¹⁴; or two adjacent R⁸ form a heterocyclyl ring;

each R^{13} and R^{14} is independently selected from H, alkyl, cycloalkyl, heterocyclalkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, arylalkyl, heteroarylalkyl, aryl, and heteroaryl; or R^{13} and R^{14} taken together form a heterocycle with the atoms to which they are attached;

Y^1 and Y^2 are O;

n is 1, 2, or 3;

m is 1;

p is 1, 2, 3, or 4;

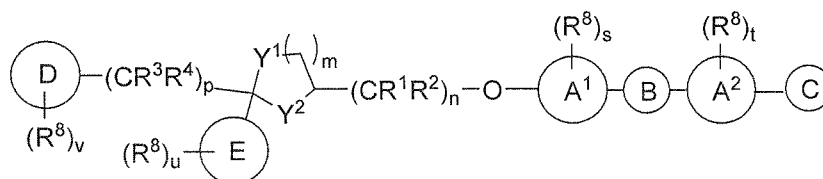
s is 0, 1, 2, 3, or 4;

t is 0, 1, 2, 3, or 4;

u is 0, 1, 2, 3, 4 or 5; and

v is 0, 1, 2, 3, or 4, in the manufacture of a medicament for treating fibrosis, a disorder characterized by fibrosis, or a disease characterized by fibrosis.

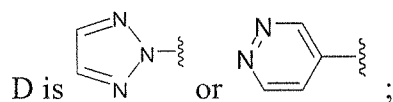
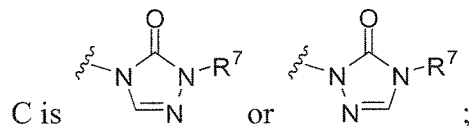
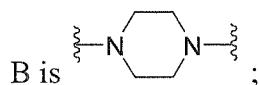
[0004b] In another aspect, there is provided a compound of Formula (II), a pharmaceutically acceptable salt, solvate, stereoisomer, or isomer thereof:



Formula (II)

wherein:

A^1 and A^2 are independently selected from aryl or heteroaryl;



E is aryl, heteroaryl, carbocyclyl, heterocyclyl, or alkyl;

each R^1 , R^2 , R^3 , and R^4 is H;

R^7 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, alkylene($NR^{13}R^{14}$), cycloalkyl, heterocyclyl, -alkylene(cycloalkyl), or -alkylene(heterocyclyl);

each R^8 is independently selected from alkyl, cycloalkyl, heterocyclyl, halo, hydroxy, nitrile, azido, nitro, alkoxy, haloalkoxy, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene($NR^{13}R^{14}$), -alkylene(cycloalkyl), -alkylene(heterocyclyl), aryl, heteroaryl, $-SR^{13}$, $-SOR^{13}$, $-SO_2R^{13}$, $-SO_2NR^{13}R^{14}$, $-NR^{13}R^{14}$, $-NR^{13}SO_2R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$, $-NR^{13}C(O)NR^{13}R^{14}$, $-C(O)R^{14}$, $-C(O)OR^{14}$, and $-C(O)NR^{13}R^{14}$; or two adjacent R^8 form a heterocyclyl ring;

each R^{13} and R^{14} is independently selected from H, alkyl, cycloalkyl, heterocyclylalkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, arylalkyl, heteroarylalkyl, aryl, and heteroaryl; or R^{13} and R^{14} taken together form a heterocycle with the atoms to which they are attached;

Y^1 and Y^2 are O;

n is 1, 2, or 3;

m is 1 or 2;

p is 1, 2, 3, or 4;

s is 0, 1, 2, 3, or 4;

t is 0, 1, 2, 3, or 4;

u is 0, 1, 2, 3, 4 or 5; and

v is 0, 1, 2, 3, or 4.

[0005] In some embodiments described above or below of a compound of Formula (I), X_1 and X_2 are N

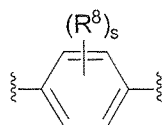
[0006] In some embodiments described above or below of a compound of Formula (I), X_1 is CR^5 and X_2 is N.

[0007] In some embodiments described above or below of a compound of Formula (I), X_1 is N and X_2 is CR^5 .

[0008] In some embodiments described above or below of a compound of Formula (I), q is 1 and r is 0.

[0009] In some embodiments described above or below of a compound of Formula (I), A^1 is aryl.

[0010] In some embodiments described above or below of a compound of Formula (I), A^1 is



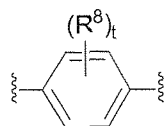
[0011] In some embodiments described above or below of a compound of Formula (I), A¹ is



[0012] In some embodiments described above or below of a compound of Formula (I), A¹ is heteroaryl.

[0013] In some embodiments described above or below of a compound of Formula (I), A² is aryl.

[0014] In some embodiments described above or below of a compound of Formula (I), A² is



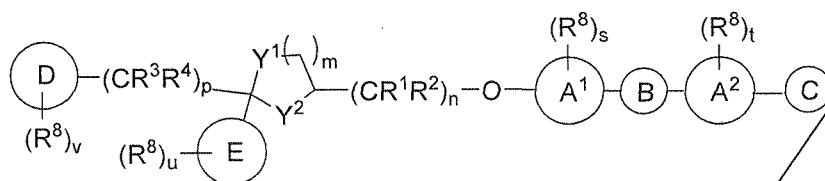
[0015] In some embodiments described above or below of a compound of Formula (I), A² is



[0016] In some embodiments described above or below of a compound of Formula (I), A² is heteroaryl.

CLAIMS

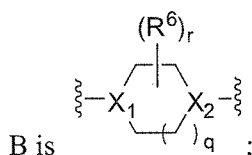
1. Use of a therapeutically effective amount of a compound of Formula (I), a pharmaceutically acceptable salt, solvate, polymorph, prodrug, metabolite, N-oxide, stereoisomer, or isomer thereof:



Formula (I)

wherein:

A¹ and A² are independently selected from aryl or heteroaryl;



C is optionally substituted 5- or 6-membered heterocyclyl or optionally substituted 5- or 6-membered heteroaryl, wherein the heterocyclyl or the heteroaryl contains 1 to 4 nitrogen atoms;

D is aryl or heteroaryl;

E is aryl, heteroaryl, carbocyclyl, heterocyclyl, or alkyl;

each R¹, R², R³, and R⁴ is independently selected from H, alkyl, haloalkyl, or alkoxy;

X₁ and X₂ are independently selected from N and CR⁵;

R⁵ is H, OH, alkyl, or alkoxy;

each R⁶ is independently alkyl, haloalkyl, halo, alkoxy, -alkylene(NR¹³R¹⁴), or aryl;

each R⁸ is independently selected from alkyl, cycloalkyl, heterocyclyl, halo, hydroxy, nitrile, azido, nitro, alkoxy, haloalkoxy, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene(NR¹³R¹⁴), -alkylene(cycloalkyl), -alkylene(heterocyclyl), aryl, heteroaryl, -SR¹³, -SOR¹³, -SO₂R¹³, -SO₂NR¹³R¹⁴, -NR¹³R¹⁴, -NR¹³SO₂R¹⁴, -NR¹³C(O)R¹⁴, -NR¹³C(O)OR¹⁴, -NR¹³C(O)NR¹³R¹⁴, -C(O)R¹⁴, -C(O)OR¹⁴, and -C(O)NR¹³R¹⁴; or two adjacent R⁸ form a heterocyclyl ring;

each R¹³ and R¹⁴ is independently selected from H, alkyl, cycloalkyl, heterocyclylalkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, arylalkyl, heteroarylalkyl, aryl,

and heteroaryl; or R¹³ and R¹⁴ taken together form a heterocycle with the atoms to which they are attached;

Y^1 and Y^2 are independently selected from O, CH_2 , NH, and NR^{13} ;

n is 1, 2, or 3;

m is 1 or 2;

p is 1, 2, 3, or 4;

q is 1, 2, or 3;

r is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

s is 0, 1, 2, 3, or 4;

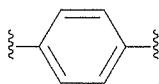
t is 0, 1, 2, 3, or 4;

u is 0, 1, 2, 3, 4 or 5; and

v is 0, 1, 2, 3, or 4, in the manufacture of a medicament for treating fibrosis, a disorder characterized by fibrosis, or a disease characterized by fibrosis.

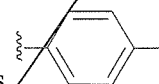
2. The use of claim 1, wherein X_1 and X_2 are N.
3. The use of claim 1, wherein X_1 is CR^5 and X_2 is N.
4. The use of claim 1, wherein X_1 is N and X_2 is CR^5 .
5. The use of any one of claims 2-4, wherein q is 1 and r is 0.
6. The use of any one of claims 1-5, wherein A^1 is aryl.

7. The use of claim 6 wherein A^1 is

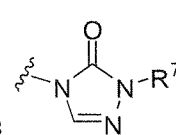


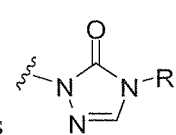
8. The use of any one of claims 1-5, wherein A^1 is heteroaryl.
9. The use of any one of claims 1-8, wherein A^2 is aryl.

10. The use of claim 9, wherein A^2 is



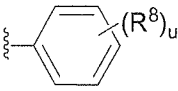
11. The use of any one of claims 1-8, wherein A^2 is heteroaryl.
12. The use of claim 11, wherein A^2 is pyridine, pyrazine, pyrimidine, pyridazine, or triazine.

13. The use of any one of claims 1-12, wherein C is ; and R^7 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene($NR^{13}R^{14}$), cycloalkyl, heterocyclyl, -alkylene(cycloalkyl), or -alkylene(heterocyclyl).

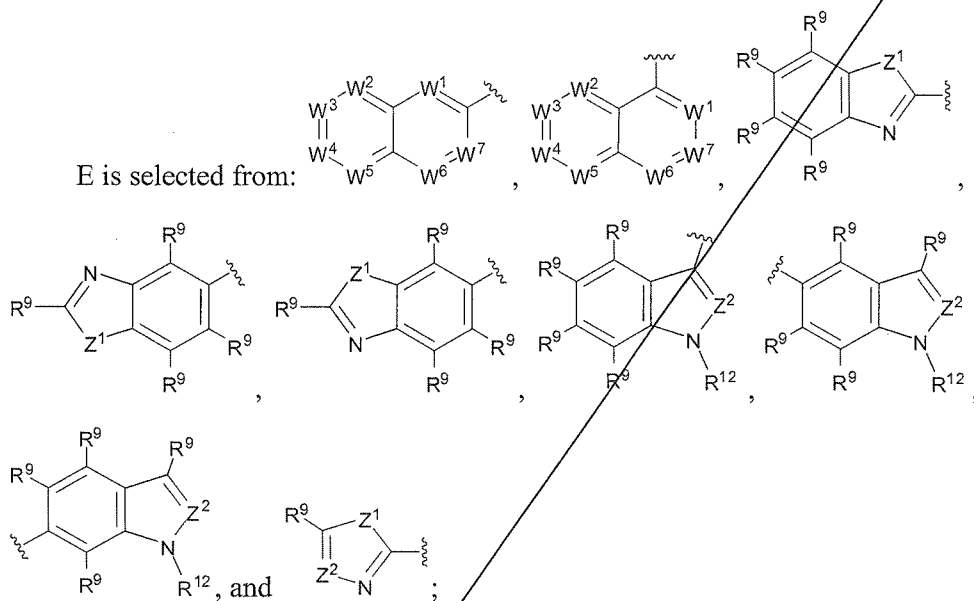
14. The use of any one of claims 1-12, wherein C is ; and R^7 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene($NR^{13}R^{14}$), cycloalkyl, heterocyclyl, -alkylene(cycloalkyl), or -alkylene(heterocyclyl).

15. The use of any one of claims 1-14, wherein E is alkyl.

16. The use of any one of claims 1-14, wherein E is cycloalkyl.
17. The use of claim 16, wherein E is cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.
18. The use of any one of claims 1-14, wherein E is heterocyclyl.
19. The use of any one of claims 1-14, wherein E is aryl.

20. The use of claim 19, wherein E is  and u is 0, 1, 2, 3, 4, or 5.
21. The use of any one of claims 1-14, wherein E is heteroaryl.
22. The use of claim 21, wherein

E is selected from:



$W^1, W^2, W^3, W^4, W^5, W^6,$ and W^7 are independently selected from N and CR^9 ;

Z^1 is NR^{12} , S, or O;

Z^2 is N or CR^9 ;

each R^9 is independently selected from H, halogen, CN, NO_2 , alkyl, $-SR^{10}$, $-OR^{10}$, $-NR^{10}R^{11}$, $NR^{10}C(O)(alkyl)$, $-NR^{10}C(O)(cycloalkyl)$, $-NR^{10}C(O)(heterocycloalkyl)$, $-NR^{10}C(O)(aryl)$, $-NR^{10}C(O)(heteroaryl)$, $-C(O)NR^{10}R^{11}$, $-C(O)NR^{10}(cycloalkyl)$, $-C(O)NR^{10}(heterocycloalkyl)$, $-C(O)NR^{10}(aryl)$, $-C(O)NR^{10}(heteroaryl)$, $-NR^{10}C(O)NR^{10}R^{11}$, $-NR^{10}C(O)NR^{10}(cycloalkyl)$, $-NR^{10}C(O)NR^{10}(heterocycloalkyl)$, $-NR^{10}C(O)NR^{10}(aryl)$, $-NR^{10}C(O)NR^{10}(heteroaryl)$, $-NR^{10}C(O)O(alkyl)$, $-NR^{10}C(O)O(cycloalkyl)$, $-NR^{10}C(O)O(heterocycloalkyl)$, $-NR^{10}C(O)O(aryl)$, $-NR^{10}C(O)O(heteroaryl)$, $-NR^{10}SO_2(alkyl)$, $-NR^{10}SO_2(cycloalkyl)$, $-NR^{10}SO_2(heterocycloalkyl)$, $-NR^{10}SO_2(aryl)$, $-NR^{10}SO_2(heteroaryl)$, $-SO_2NR^{10}R^{11}$, $-SO_2NR^{10}(cycloalkyl)$, $-SO_2NR^{10}(heterocycloalkyl)$, $-SO_2NR^{10}(aryl)$, $-SO_2NR^{10}(heteroaryl)$, haloalkyl, aryl, and heteroaryl;

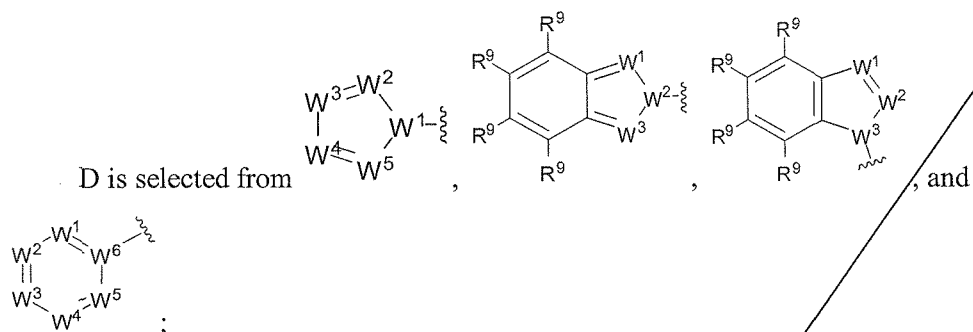
each R^{10} and R^{11} is independently selected from H and alkyl; or R^{10} and R^{11} taken together form a heterocycle with the nitrogen to which they are attached; and

R^{12} is H, alkyl or haloalkyl.

23. The use of any one of claims 1-22, wherein D is aryl.

24. The use of any one of claims 1-22, wherein D is heteroaryl.

25. The use of claim 24, wherein



W^1 , W^2 , W^3 , W^4 , and W^5 are independently selected from N and CR^9 ;

W^6 is N or C; and

each R^9 is independently selected from H, halogen, CN, NO_2 ,

alkyl, $-SR^{10}$, $-OR^{10}$, $-NR^{10}R^{11}$,

$NR^{10}C(O)(alkyl)$, $-NR^{10}C(O)(cycloalkyl)$, $-NR^{10}C(O)(heterocycloalkyl)$, $-NR^{10}C(O)(aryl)$, $-NR^{10}C(O)(heteroaryl)$, $-C(O)NR^{10}R^{11}$, $-C(O)NR^{10}(cycloalkyl)$, $-C(O)NR^{10}(heterocycloalkyl)$, $-C(O)NR^{10}(aryl)$, $-C(O)NR^{10}(heteroaryl)$, $-NR^{10}C(O)NR^{10}R^{11}$, $-NR^{10}C(O)NR^{10}(cycloalkyl)$, $-NR^{10}C(O)NR^{10}(heterocycloalkyl)$, $-NR^{10}C(O)NR^{10}(aryl)$, $-NR^{10}C(O)NR^{10}(heteroaryl)$, $-NR^{10}C(O)O(alkyl)$, $-NR^{10}C(O)O(cycloalkyl)$, $-NR^{10}C(O)O(heterocycloalkyl)$, $-NR^{10}C(O)O(aryl)$, $-NR^{10}C(O)O(heteroaryl)$, $-NR^{10}SO_2(alkyl)$, $-NR^{10}SO_2(cycloalkyl)$, $-NR^{10}SO_2(heterocycloalkyl)$, $-NR^{10}SO_2(aryl)$, $-NR^{10}SO_2(heteroaryl)$, $-SO_2NR^{10}R^{11}$, $-SO_2NR^{10}(cycloalkyl)$, $-SO_2NR^{10}(heterocycloalkyl)$, $-SO_2NR^{10}(aryl)$, $-SO_2NR^{10}(heteroaryl)$, haloalkyl, aryl, and heteroaryl.

26. The use of any one of claims 1-25 wherein Y^1 and Y^2 are O.

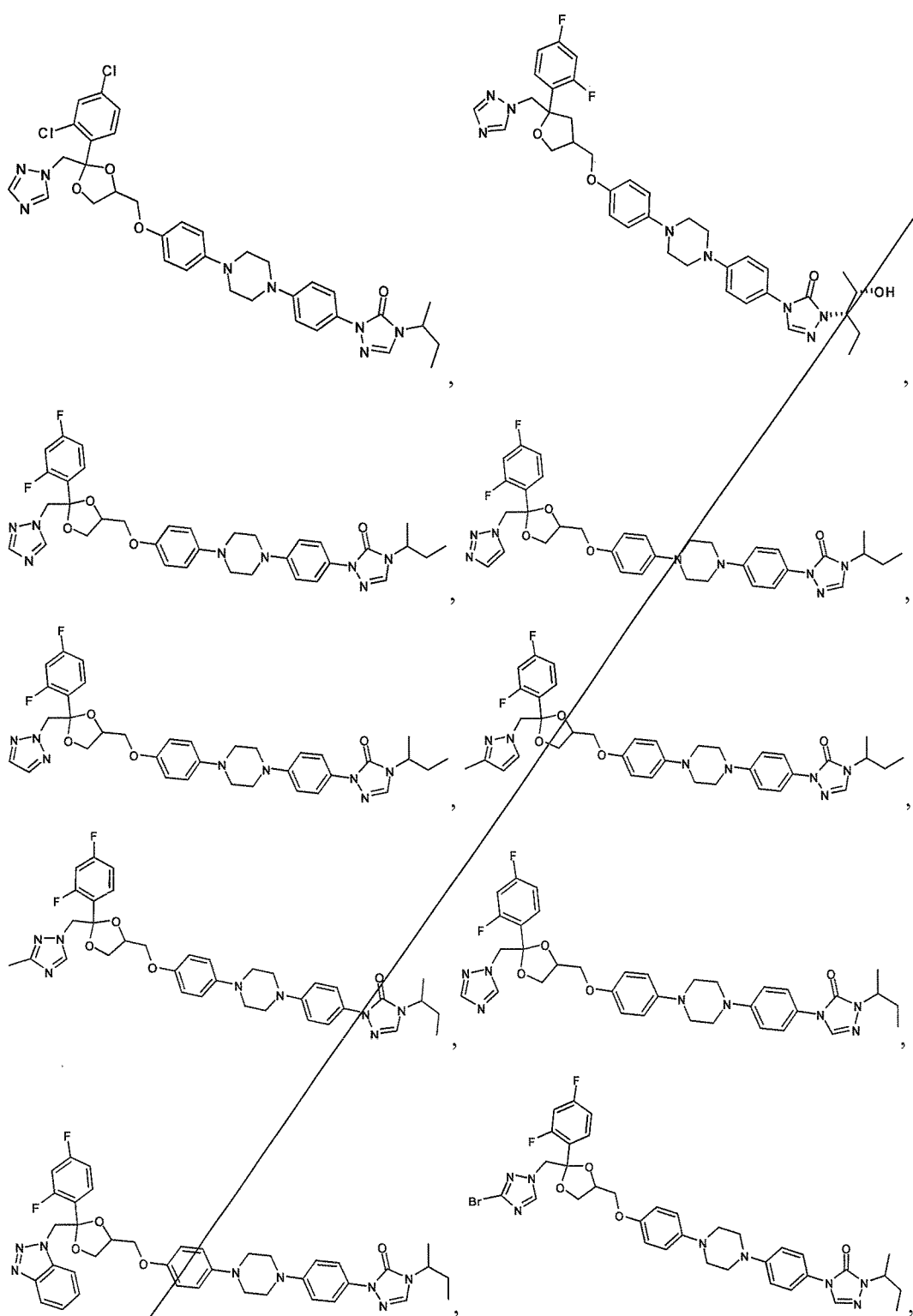
27. The use of claim 26 wherein m is 1.

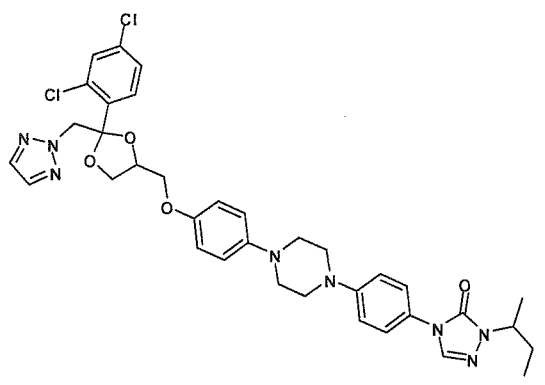
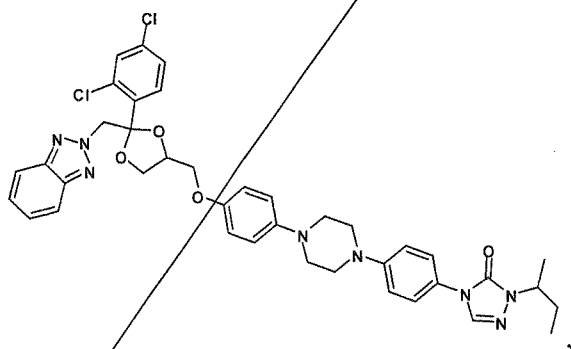
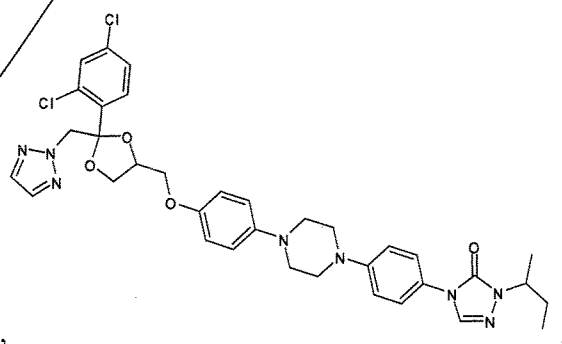
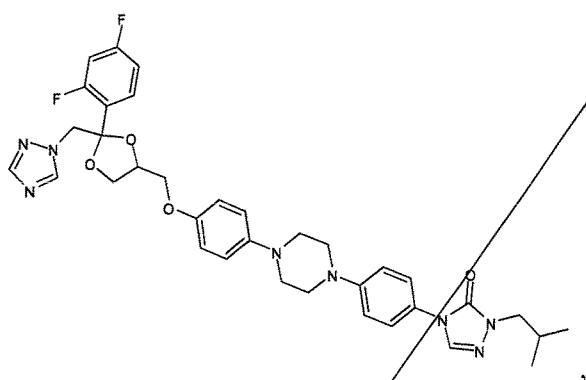
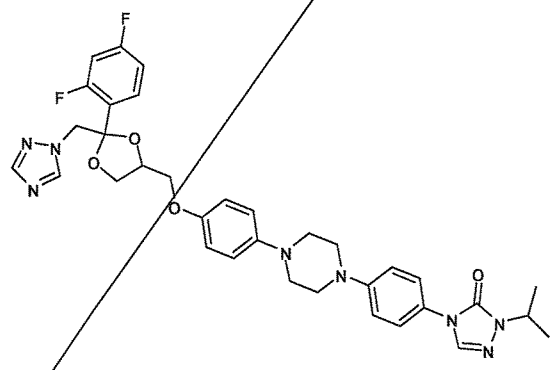
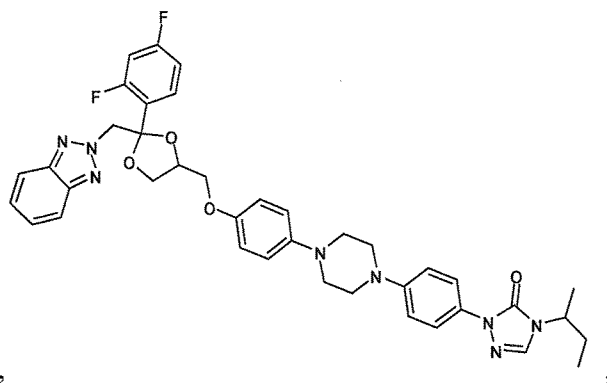
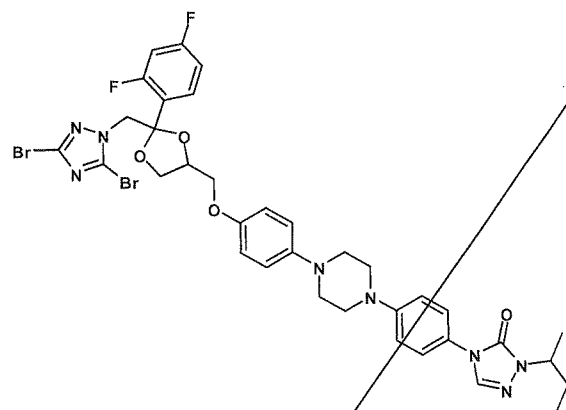
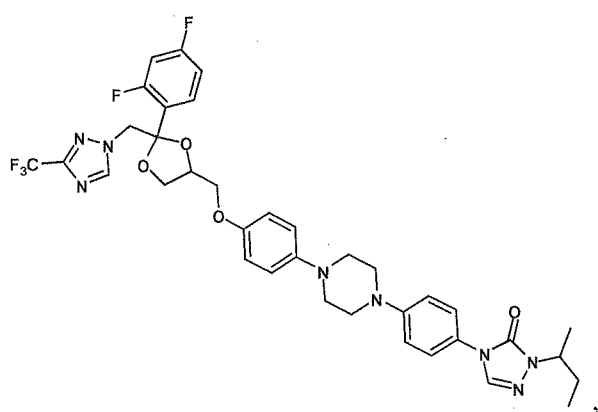
28. The use of any one of claims 1-27 wherein p is 1, 2, or 3.

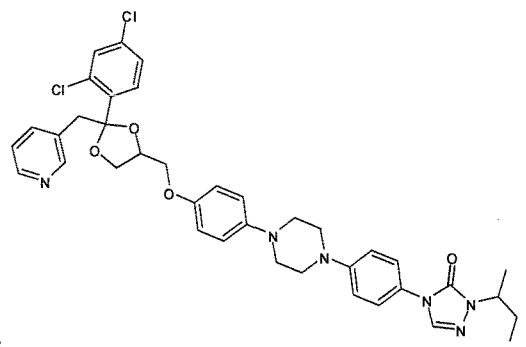
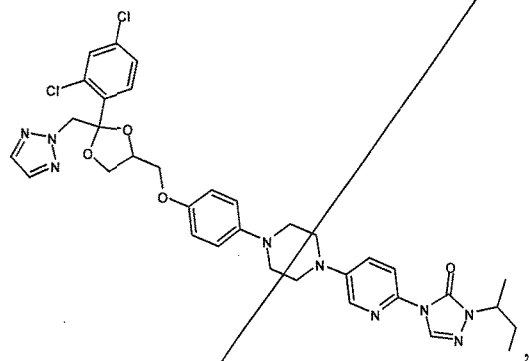
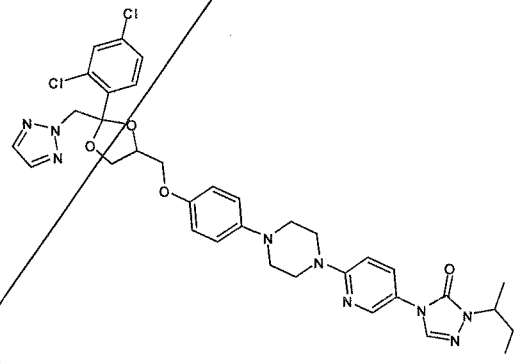
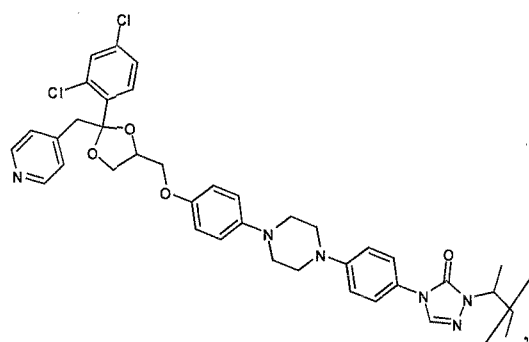
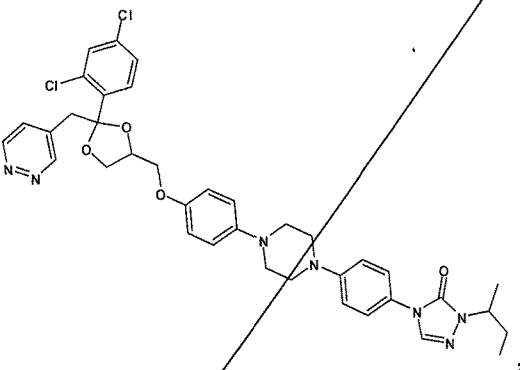
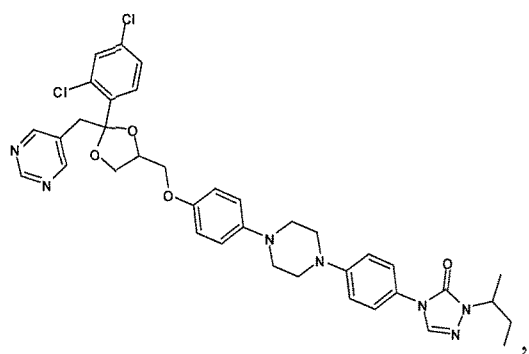
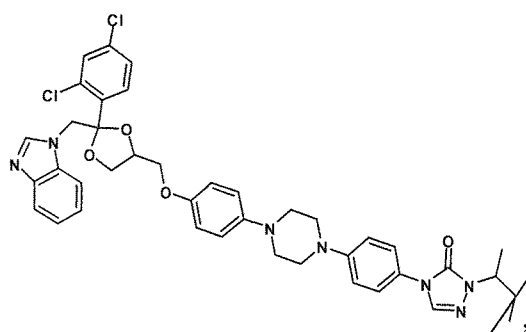
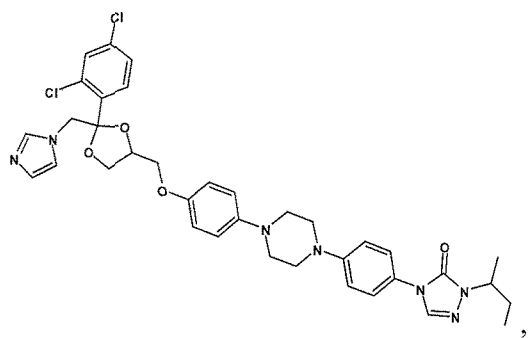
29. The use of claim 28 wherein p is 1.

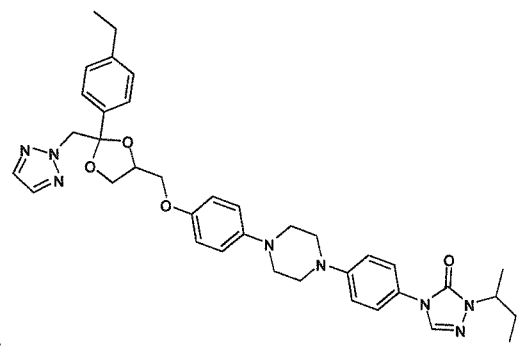
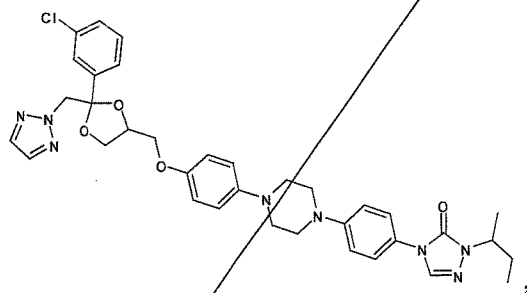
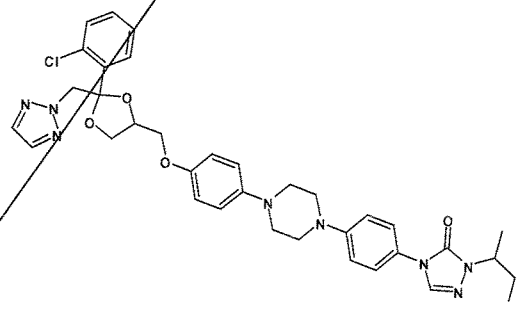
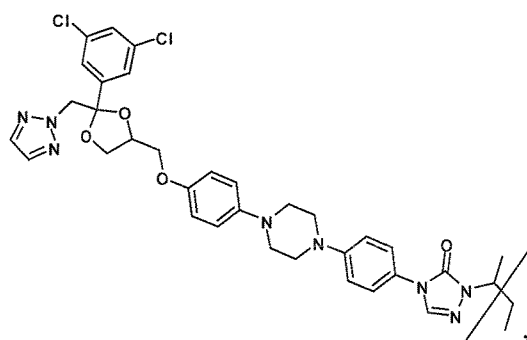
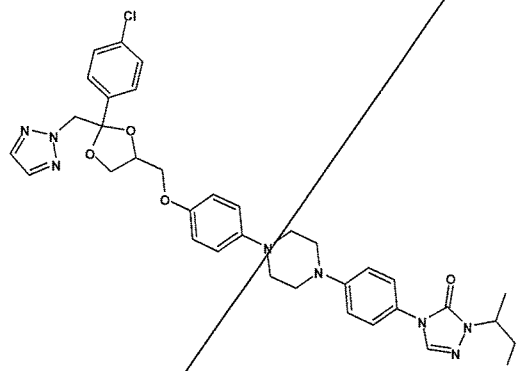
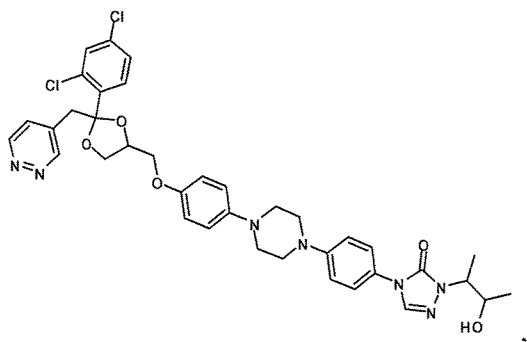
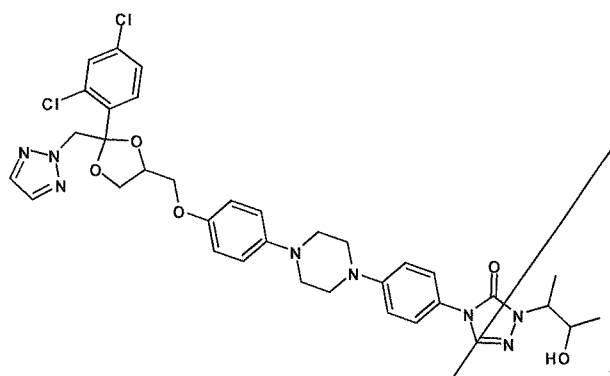
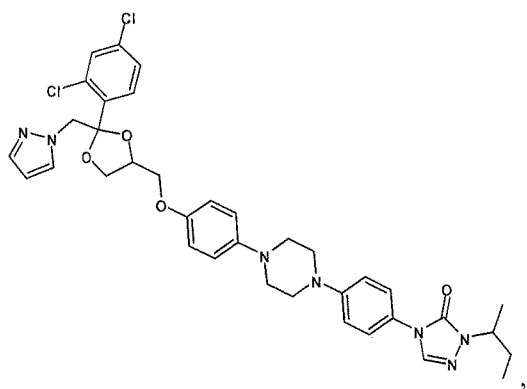
30. The use of any one of claims 1-29 wherein R^1 , R^2 , R^3 , and R^4 are hydrogen.

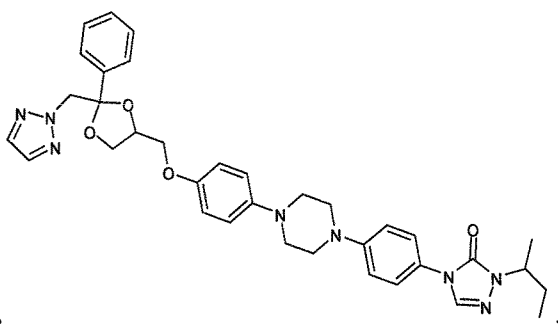
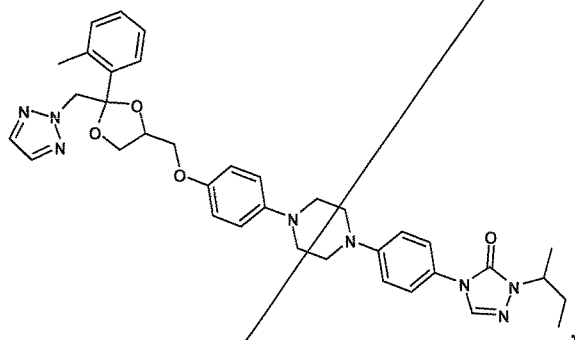
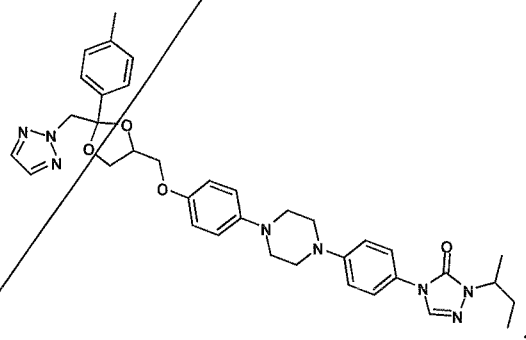
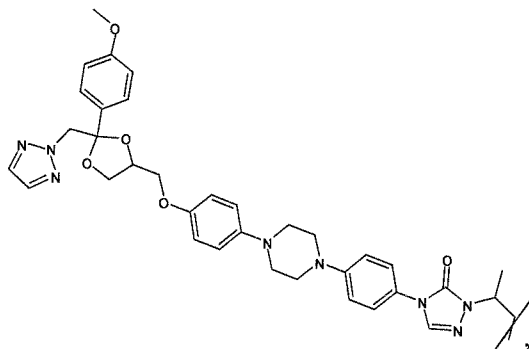
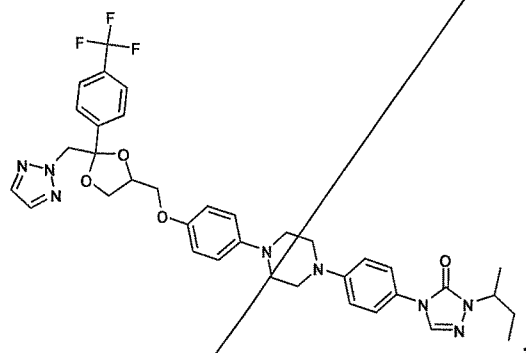
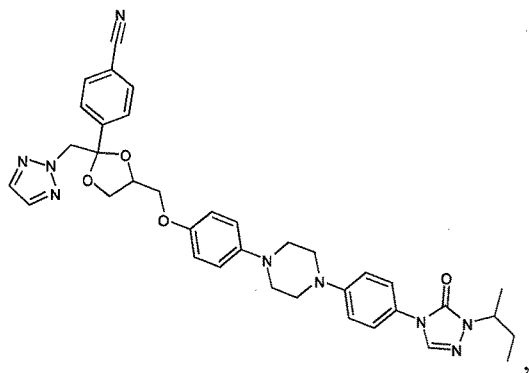
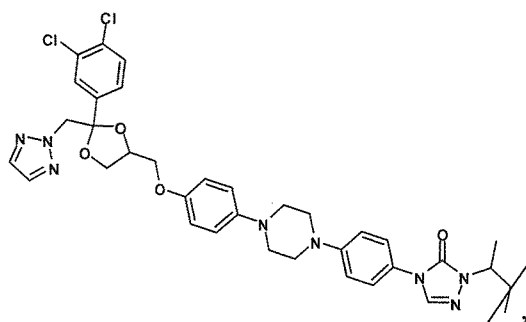
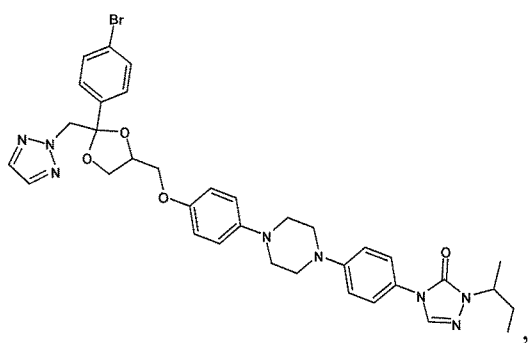
31. The use of claim 1 wherein the compound is selected from:

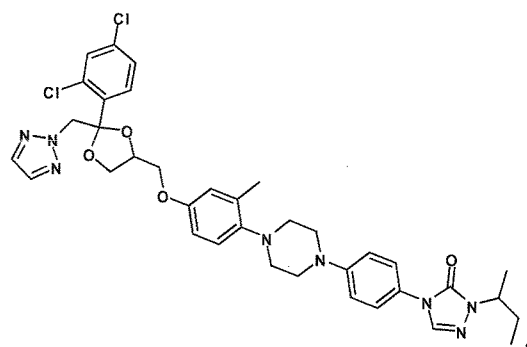
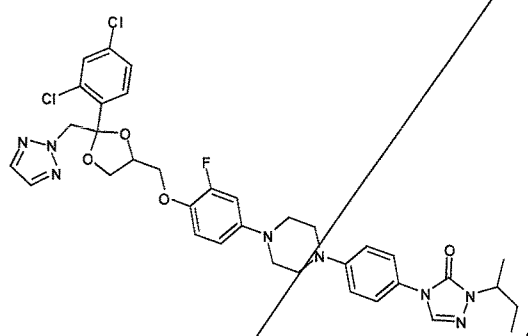
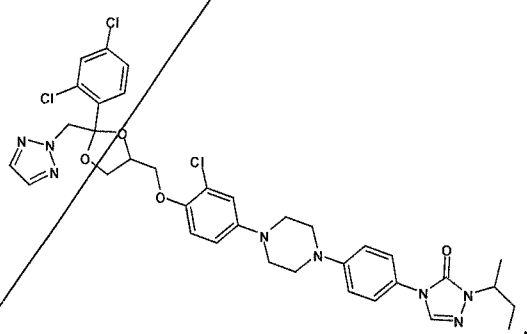
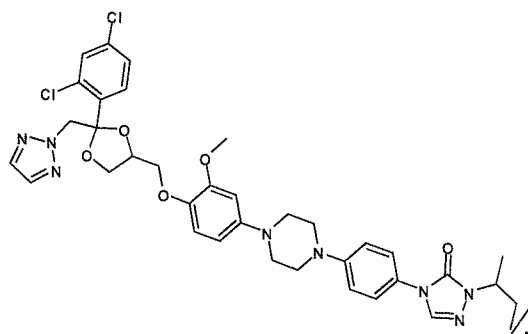
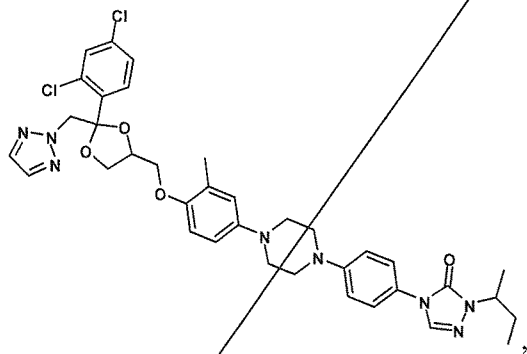
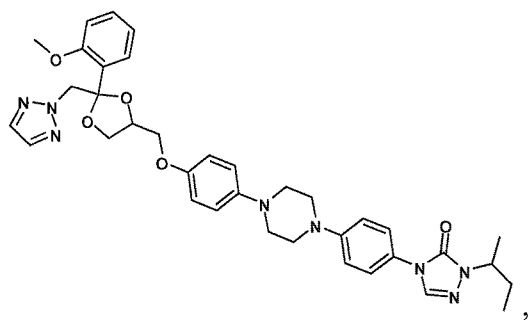
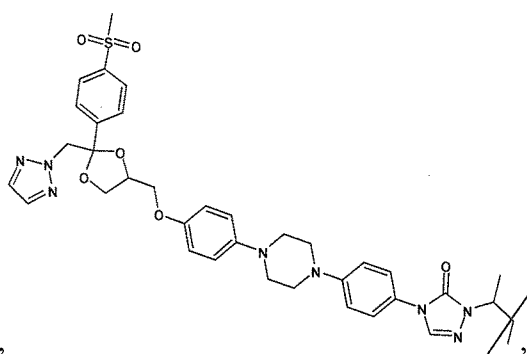
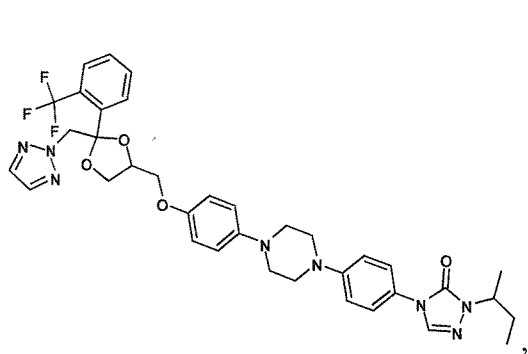


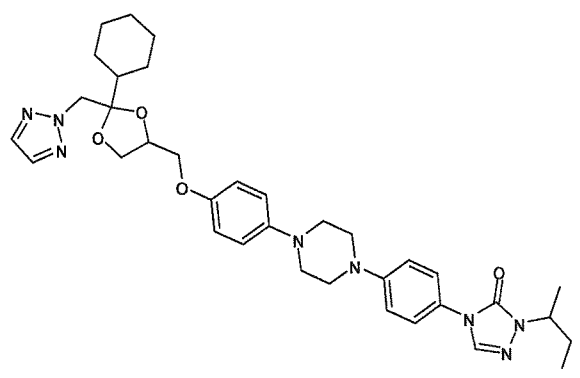
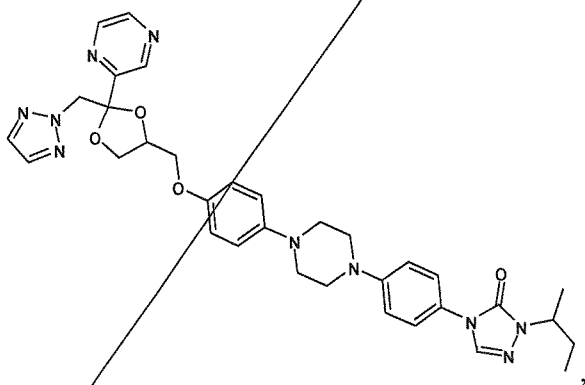
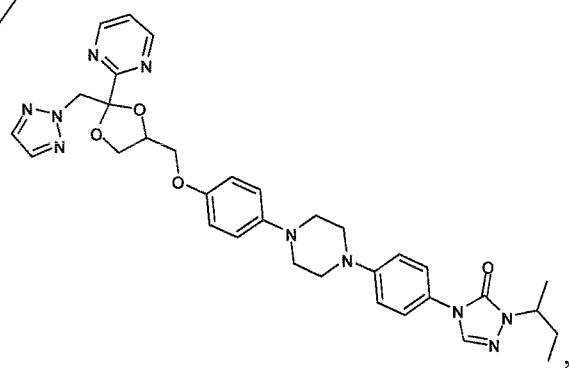
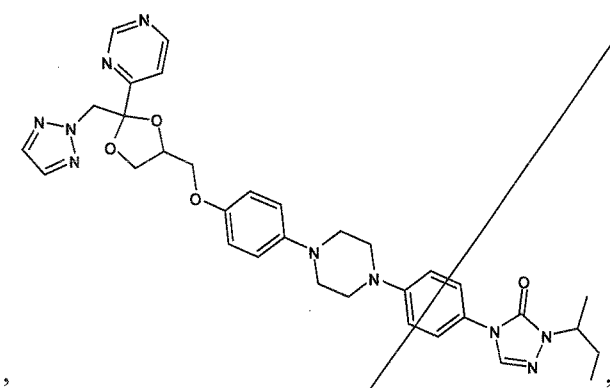
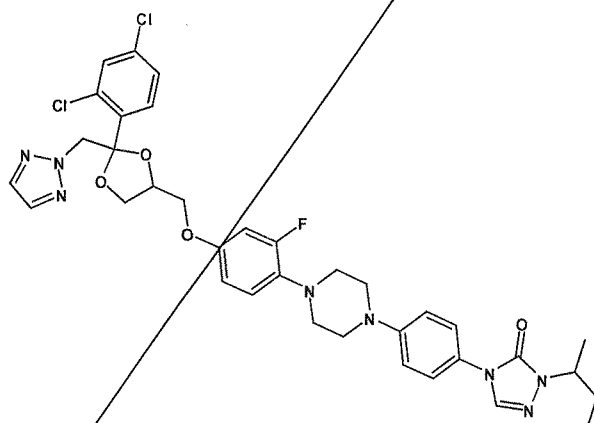
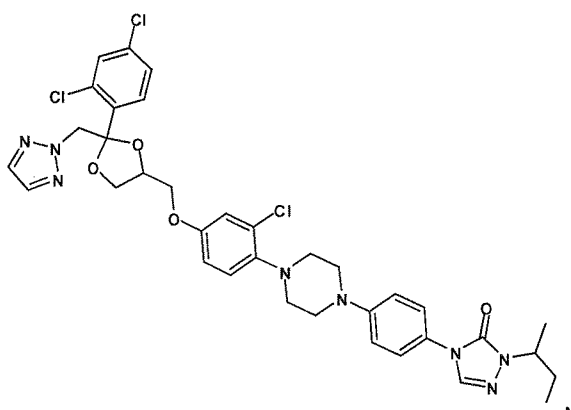
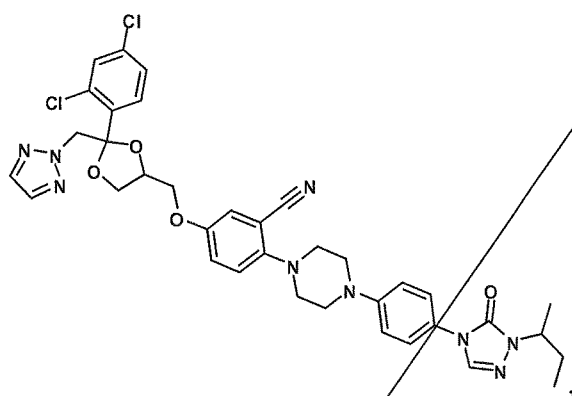
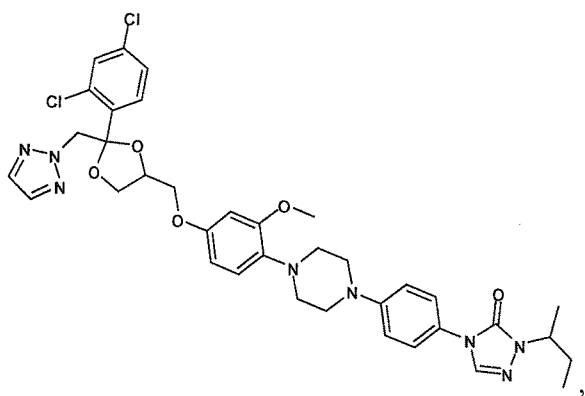


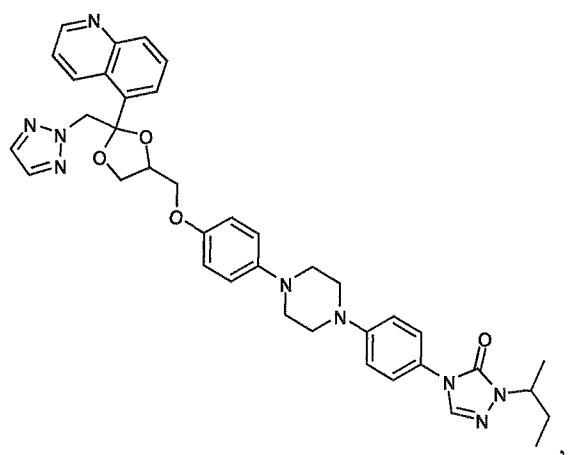
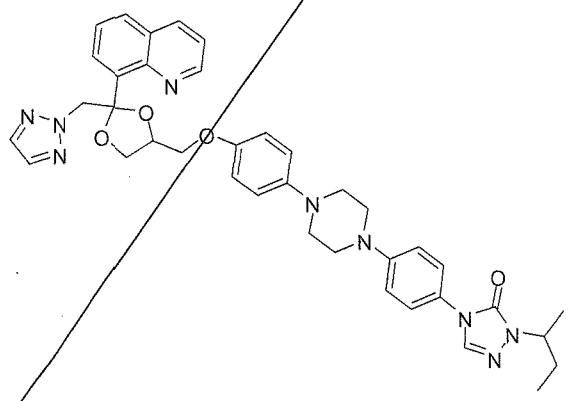
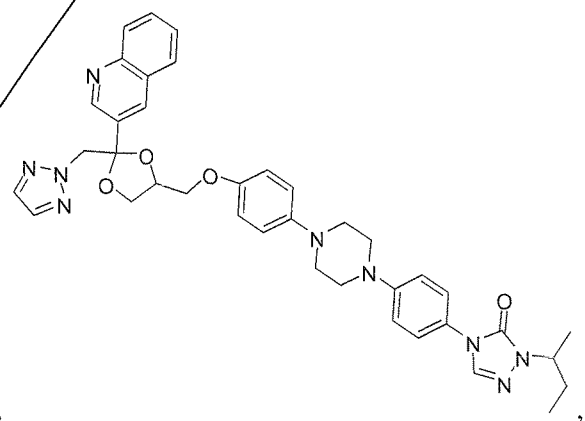
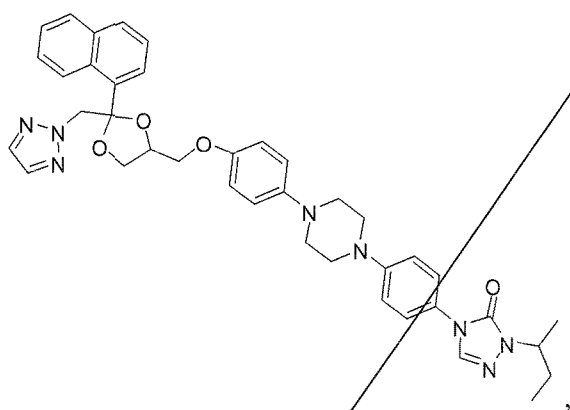
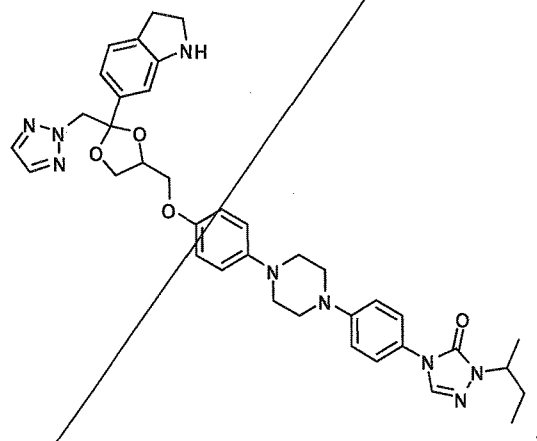
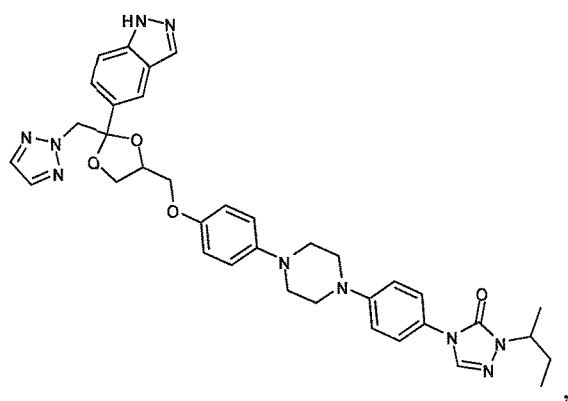
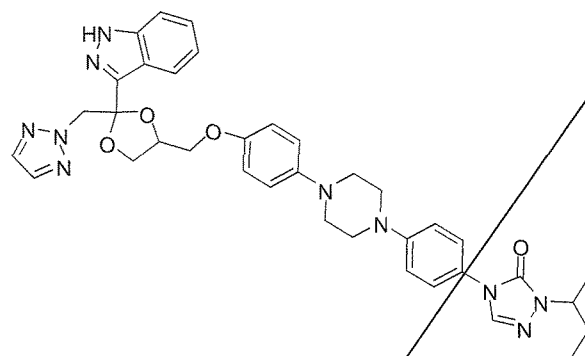
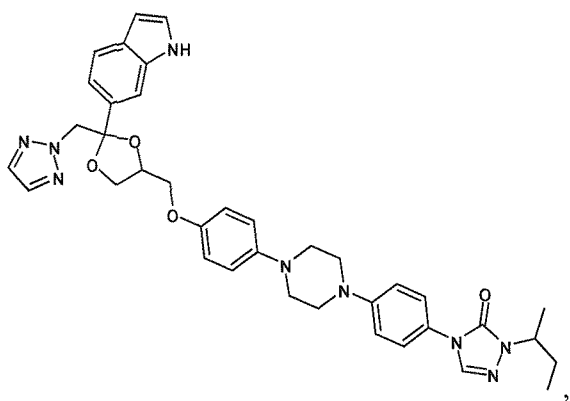


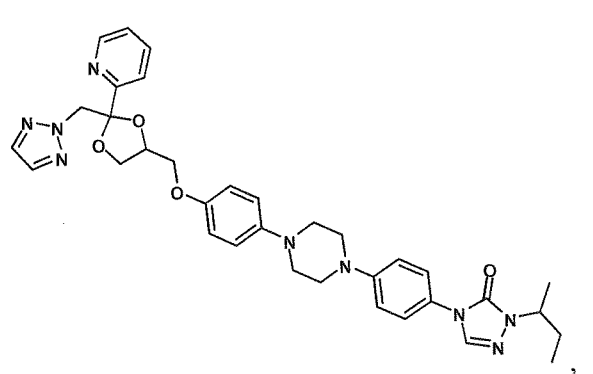
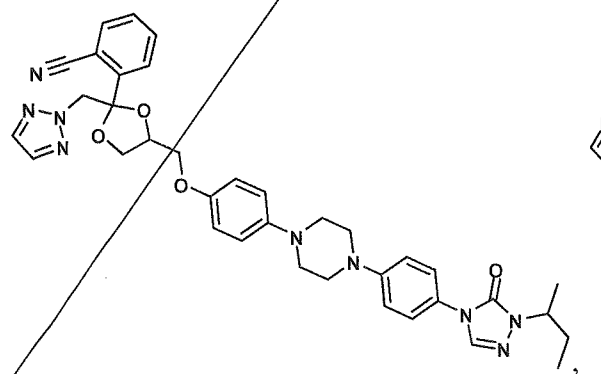
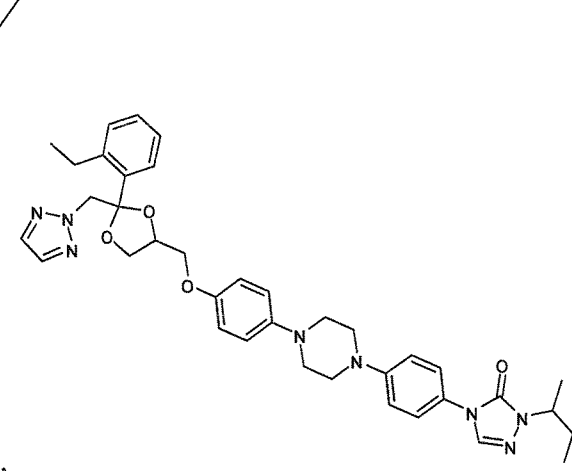
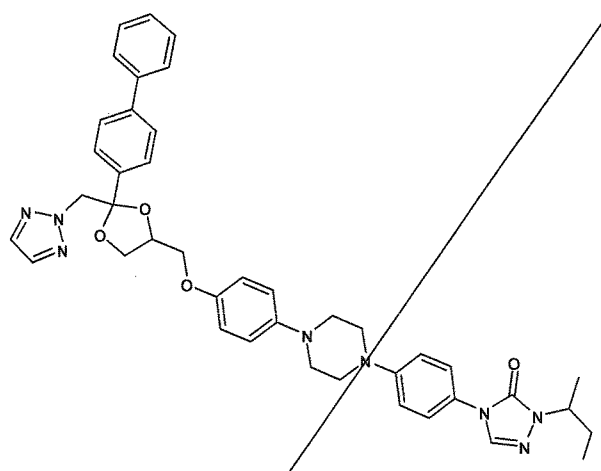
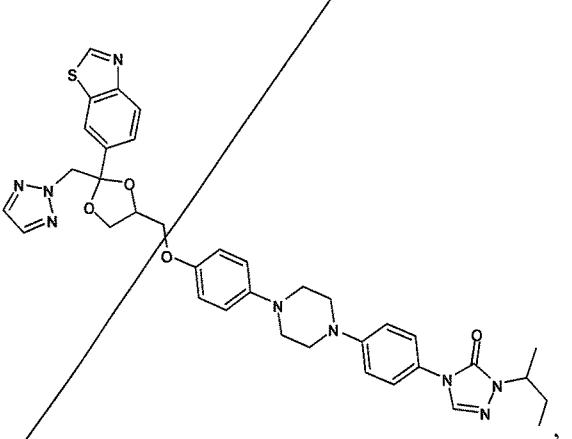
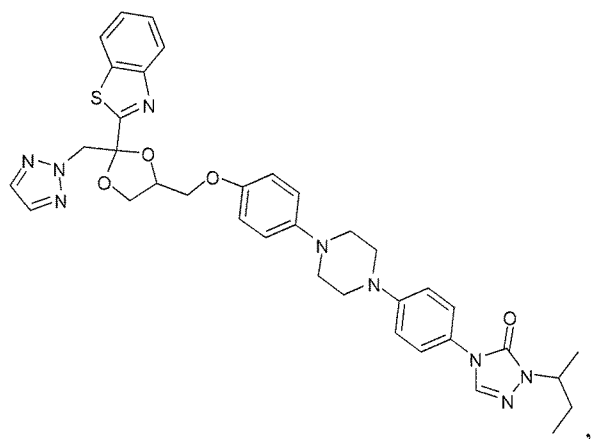
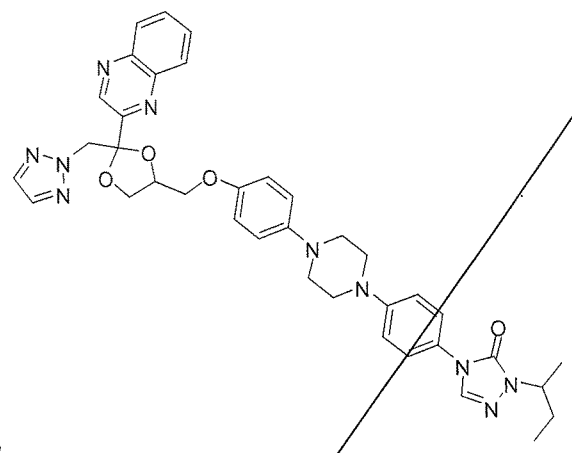
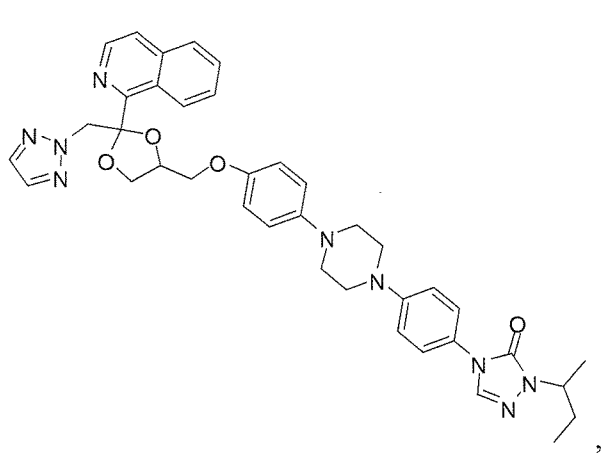


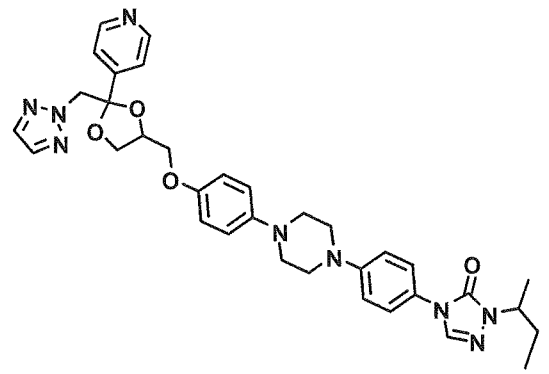
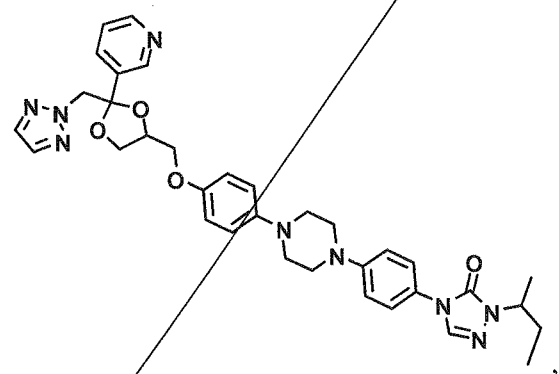
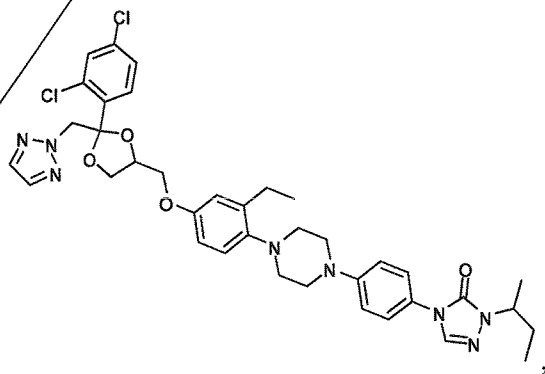
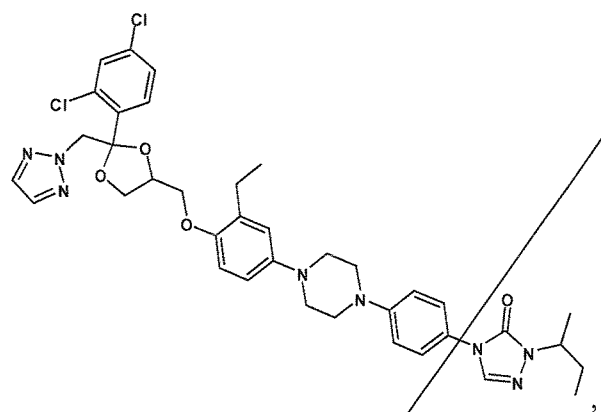
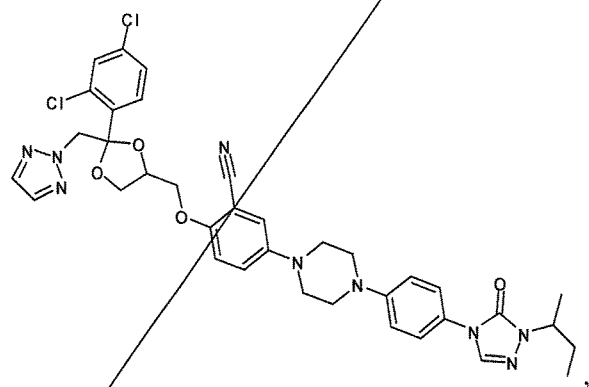
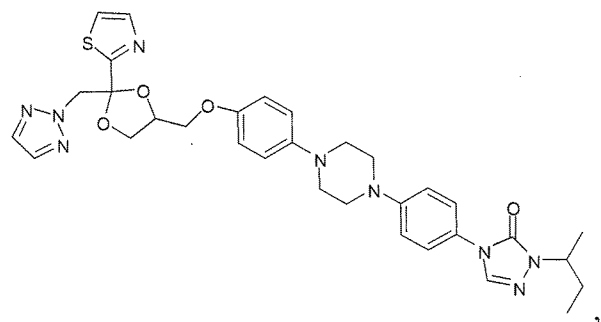
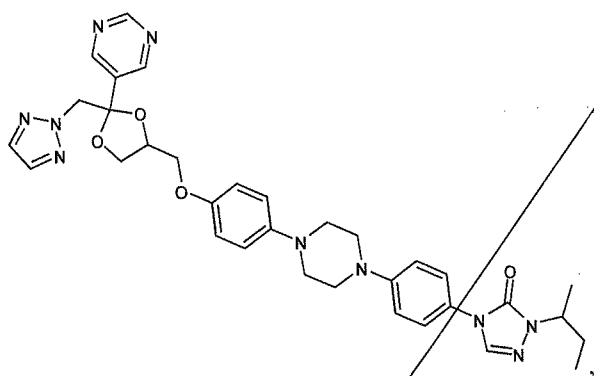
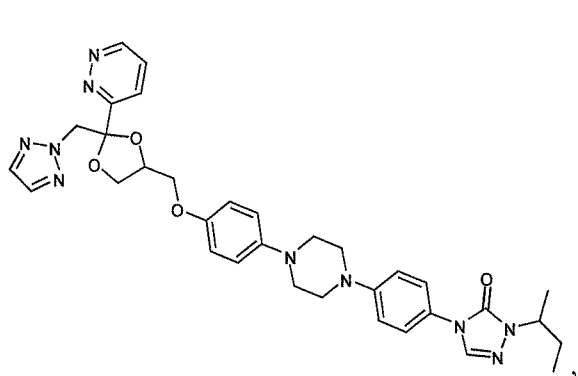


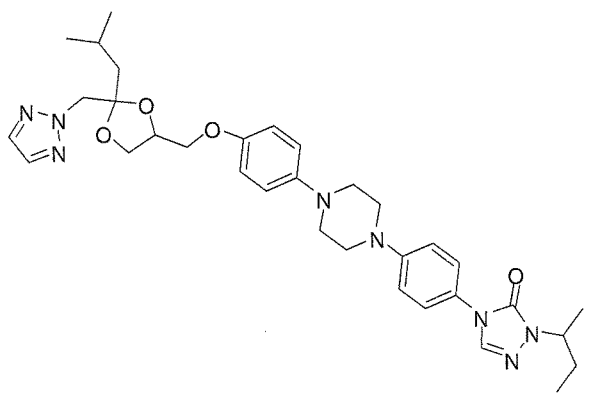
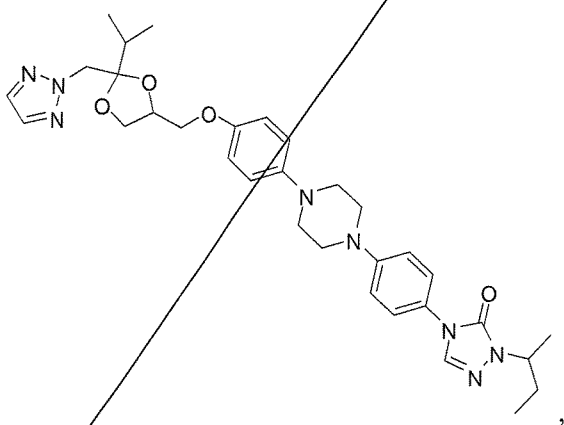
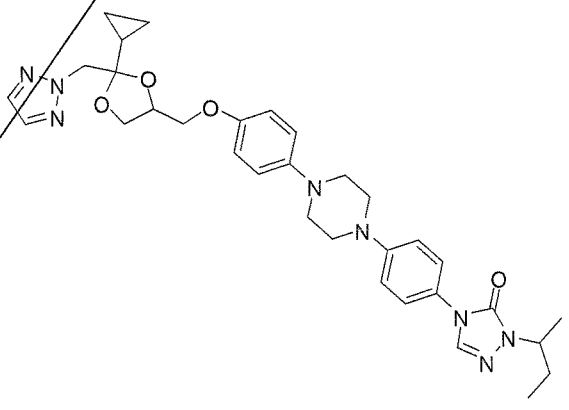
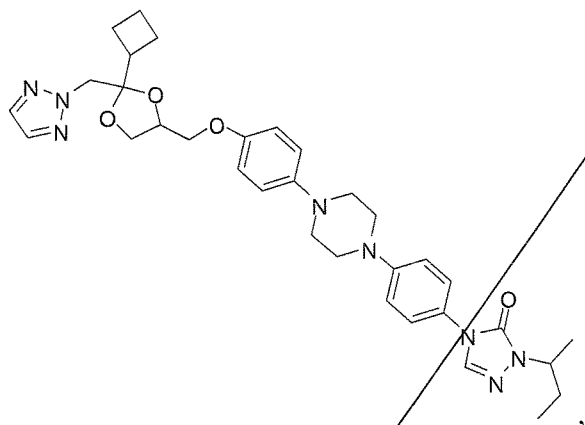
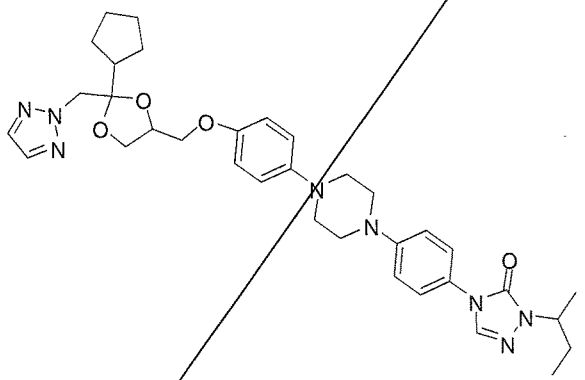
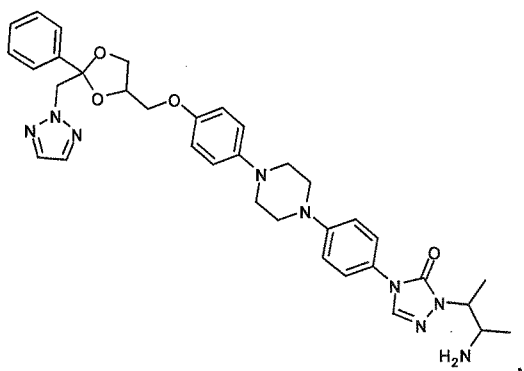
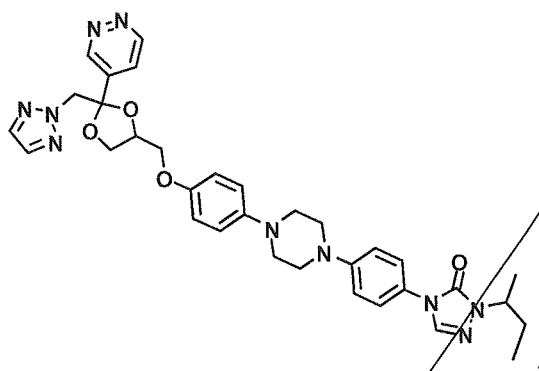
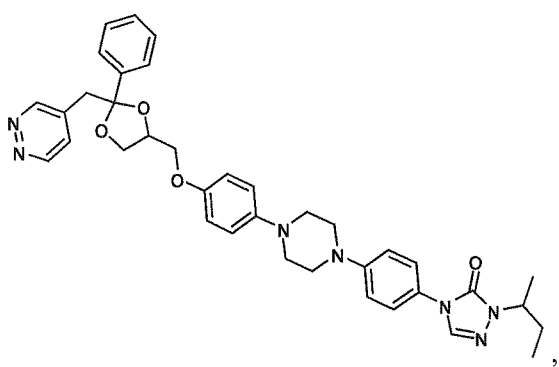


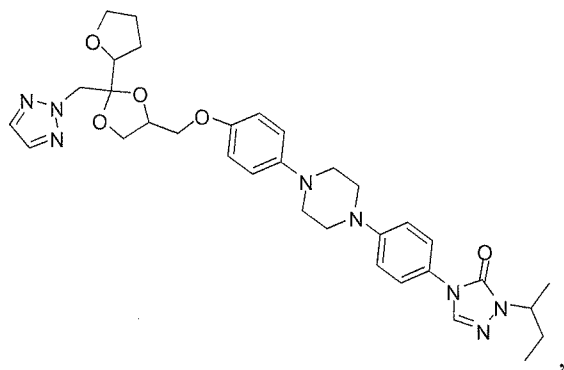
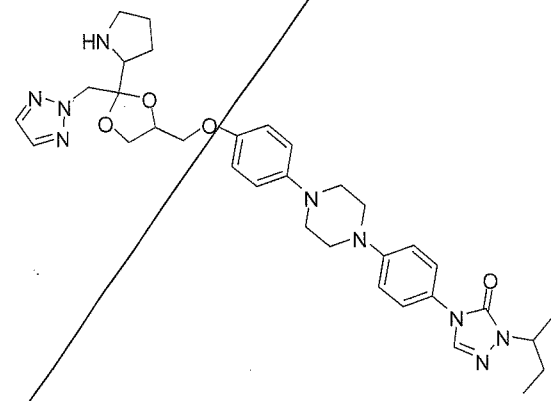
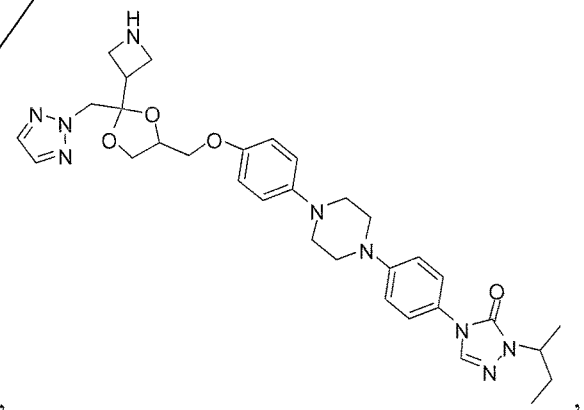
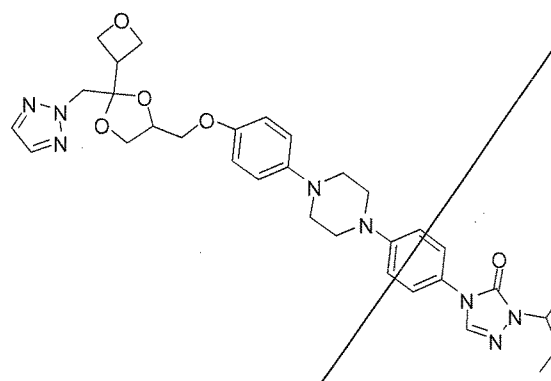
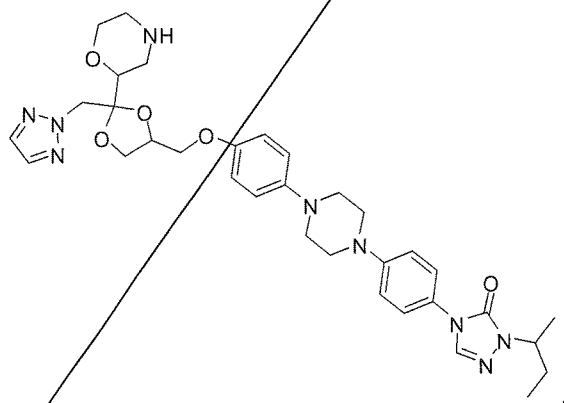
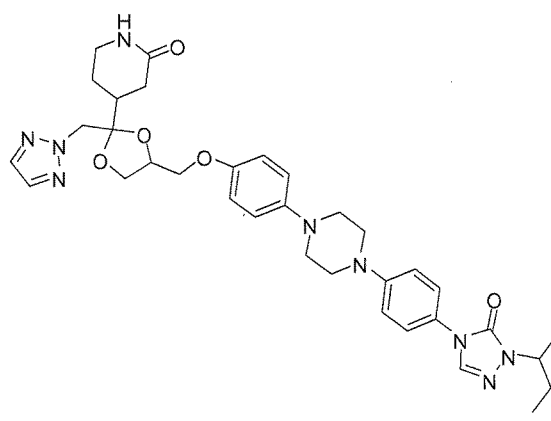
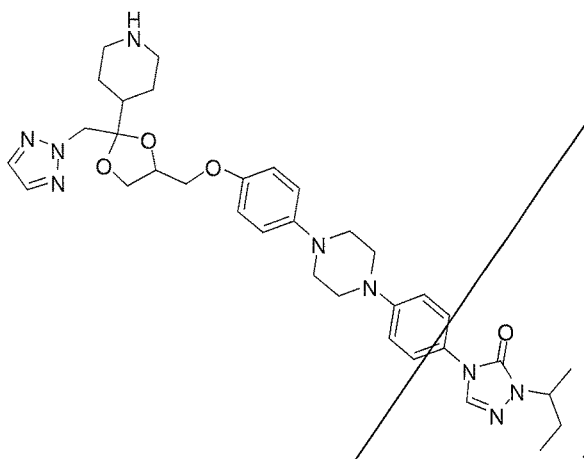
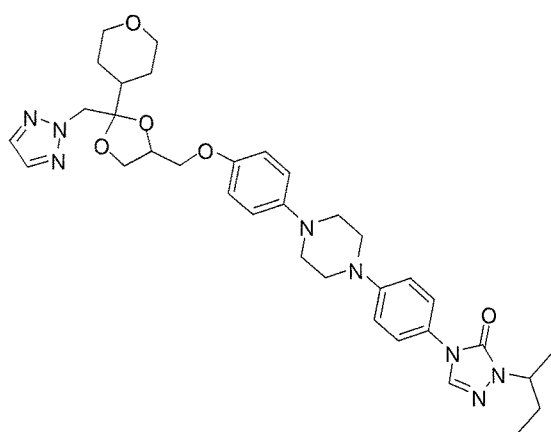


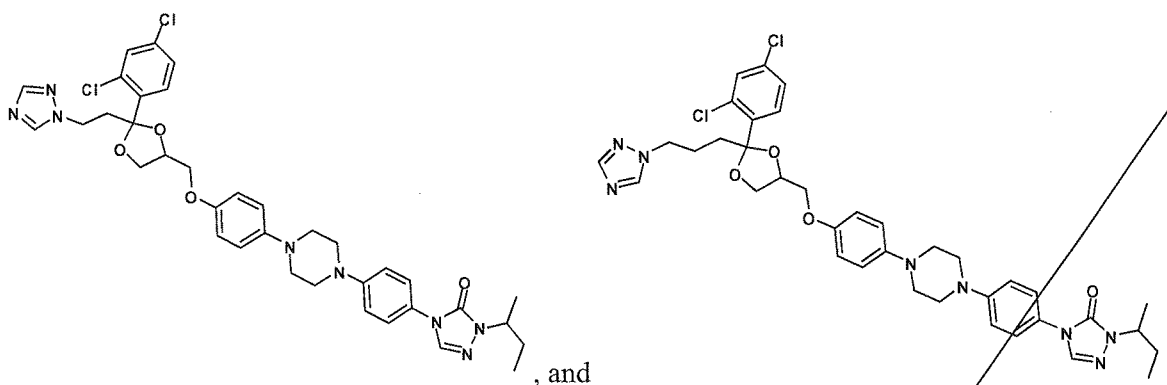




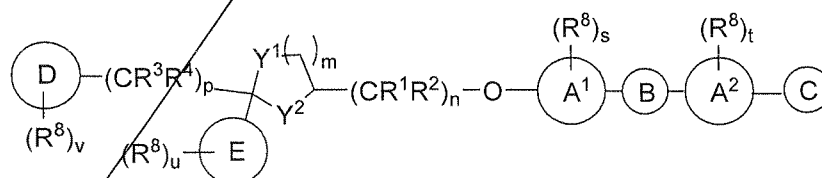








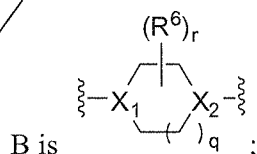
32. The use of any one of claims 1-31 wherein the fibrosis is liver fibrosis, idiopathic pulmonary fibrosis, kidney fibrosis, or cardiac fibrosis.
33. The use of claim 32 wherein the liver fibrosis is associated with the later stages of alcoholic or nonalcoholic liver cirrhosis.
34. The use of claim 32 wherein the fibrosis is idiopathic pulmonary fibrosis.
35. The use of any one of claims 1-31 wherein the disease or disorder characterized by fibrosis is a chronic autoimmune disease.
36. The use of claim 35 wherein the chronic autoimmune disease is rheumatoid arthritis, scleroderma, Crohn's disease or systemic lupus erythematosus.
37. The use of claim 36 wherein the chronic autoimmune disease is scleroderma.
38. The use of any one of claims 1-31 wherein the fibrosis is keloid formation resulting from abnormal wound healing.
39. The use of any one of claims 1-31 wherein the fibrosis occurs after organ transplantation.
40. A compound of Formula (II), a pharmaceutically acceptable salt, solvate, polymorph, prodrug, metabolite, N-oxide, stereoisomer, or isomer thereof:



Formula (II)

wherein:

A¹ and A² are independently selected from aryl or heteroaryl;



C is optionally substituted 5- or 6-membered heterocyclyl or optionally substituted 5- or 6-membered heteroaryl, wherein the heterocyclyl or the heteroaryl contains 1 to 4 nitrogen atoms;

D is aryl or heteroaryl;

E is aryl, heteroaryl, carbocyclyl, heterocyclyl, or alkyl;

each R^1 , R^2 , R^3 , and R^4 is independently selected from H, alkyl, haloalkyl, or alkoxy;

X_1 and X_2 are independently selected from N and CR^5 ;

R^5 is H, OH, alkyl, or alkoxy;

each R^6 is independently alkyl, haloalkyl, halo, alkoxy, -alkylene($NR^{13}R^{14}$), or aryl;

R^7 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene($NR^{13}R^{14}$), cycloalkyl, heterocyclyl, -alkylene(cycloalkyl), or -alkylene(heterocyclyl);

each R^8 is independently selected from alkyl, cycloalkyl, heterocyclyl, halo, hydroxy, nitrile, azido, nitro, alkoxy, haloalkoxy, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene($NR^{13}R^{14}$), -alkylene(cycloalkyl), -alkylene(heterocyclyl), aryl, heteroaryl, $-SR^{13}$, $-SOR^{13}$, $-SO_2R^{13}$, $-SO_2NR^{13}R^{14}$, $-NR^{13}R^{14}$, $-NR^{13}SO_2R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$, $-NR^{13}C(O)NR^{13}R^{14}$, $-C(O)R^{14}$, $-C(O)OR^{14}$, and $-C(O)NR^{13}R^{14}$; or two adjacent R^8 form a heterocyclyl ring;

each R^{13} and R^{14} is independently selected from H, alkyl, cycloalkyl, heterocyclylalkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, arylalkyl, heteroarylalkyl, aryl, and heteroaryl; or R^{13} and R^{14} taken together form a heterocycle with the atoms to which they are attached;

Y^1 and Y^2 are independently selected from O, CH_2 , NH, and NR^{13} ;

n is 1, 2, or 3;

m is 1 or 2;

p is 1, 2, 3, or 4;

q is 1, 2, or 3;

r is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

s is 0, 1, 2, 3, or 4;

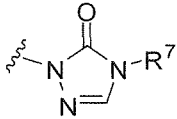
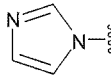
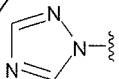
t is 0, 1, 2, 3, or 4;

u is 0, 1, 2, 3, 4 or 5; and

v is 0, 1, 2, 3, or 4;

provided that:

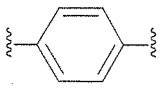
if X_1 and X_2 are N; r is 0; q is 1; A^1 and A^2 are phenyl; Y^1 and Y^2 are O; m and n are 1;

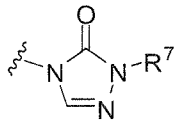
R^1 , R^2 , R^3 , and R^4 are hydrogen; and C is , then D is not  or ; and

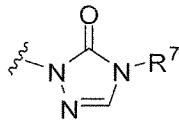
the compound is not 4-(4-(4-(4-((2-((1H-pyrazol-1-yl)methyl)-2-(2,4-difluorophenyl)-1,3-dioxolan-4-yl)methoxy)phenyl)piperazin-1-yl)phenyl)-1-isopropyl-1H-1,2,4-triazol-5(4H)-one.

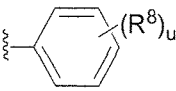
41. The compound of claim 40, wherein X_1 and X_2 are N.
42. The compound of claim 40, wherein X_1 is CR^5 and X_2 is N.
43. The compound of claim 40, wherein X_1 is N and X_2 is CR^5 .
44. The compound of any one of claims 40-43, wherein q is 1 and r is 0.
45. The compound of any one of claims 40-44, wherein A^1 is aryl.

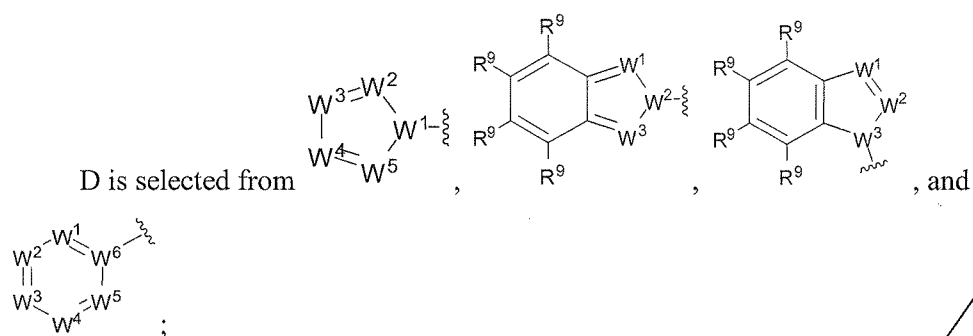
46. The compound of claim 45 wherein A^1 is .
47. The compound of any one of claims 40-44, wherein A^1 is heteroaryl.
48. The compound of any one of claims 40-47, wherein A^2 is aryl.

49. The compound of claim 48, wherein A^2 is .
50. The compound of any one of claims 40-47, wherein A^2 is heteroaryl.
51. The compound of claim 50, wherein A^2 is pyridine, pyrazine, pyrimidine, pyridazine, or triazine.

52. The compound of any one of claims 40-51, wherein C is .

53. The compound of any one of claims 40-51, wherein C is .
54. The compound of any one of claims 40-53, wherein E is alkyl.
55. The compound of any one of claims 40-53, wherein E is cycloalkyl.
56. The compound of claim 55, wherein E is cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.
57. The compound of any one of claims 40-53, wherein E is heterocyclyl.
58. The compound of any one of claims 40-53, wherein E is aryl.

59. The compound of claim 58, wherein E is  and u is 0, 1, 2, 3, 4, or 5.
60. The compound of any one of claims 40-53, wherein E is heteroaryl.
61. The compound of claim 60, wherein



W^1 , W^2 , W^3 , W^4 , and W^5 are independently selected from N and CR^9 ;

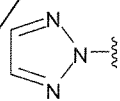
W^6 is N or C; and

each R^9 is independently selected from H, halogen, CN, NO_2 ,

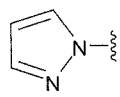
alkyl, $-SR^{10}$, $-OR^{10}$, $-NR^{10}R^{11}$,

$NR^{10}C(O)(alkyl)$, $-NR^{10}C(O)(cycloalkyl)$, $-NR^{10}C(O)(heterocycloalkyl)$, $-NR^{10}C(O)(aryl)$, $-NR^{10}C(O)(heteroaryl)$, $-C(O)NR^{10}R^{11}$, $-C(O)NR^{10}(cycloalkyl)$, $-C(O)NR^{10}(heterocycloalkyl)$, $-C(O)NR^{10}(aryl)$, $-C(O)NR^{10}(heteroaryl)$, $-NR^{10}C(O)NR^{10}R^{11}$, $-NR^{10}C(O)NR^{11}(cycloalkyl)$, $-NR^{10}C(O)NR^{11}(heterocycloalkyl)$, $-NR^{10}C(O)NR^{11}(aryl)$, $-NR^{10}C(O)NR^{11}(heteroaryl)$, $-NR^{10}C(O)O(alkyl)$, $-NR^{10}C(O)O(cycloalkyl)$, $-NR^{10}C(O)O(heterocycloalkyl)$, $-NR^{10}C(O)O(aryl)$, $-NR^{10}C(O)O(heteroaryl)$, $-NR^{10}SO_2(alkyl)$, $-NR^{10}SO_2(cycloalkyl)$, $-NR^{10}SO_2(heterocycloalkyl)$, $-NR^{10}SO_2(aryl)$, $-NR^{10}SO_2(heteroaryl)$, $-SO_2NR^{10}R^{11}$, $-SO_2NR^{10}(cycloalkyl)$, $-SO_2NR^{10}(heterocycloalkyl)$, $-SO_2NR^{10}(aryl)$, $-SO_2NR^{10}(heteroaryl)$, haloalkyl, aryl, and heteroaryl.

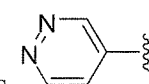
65. The compound of claim 64, wherein D is



66. The compound of claim 64, wherein D is



67. The compound of claim 64, wherein D is



68. The compound of any one of claims 40-67 wherein Y^1 and Y^2 are O.

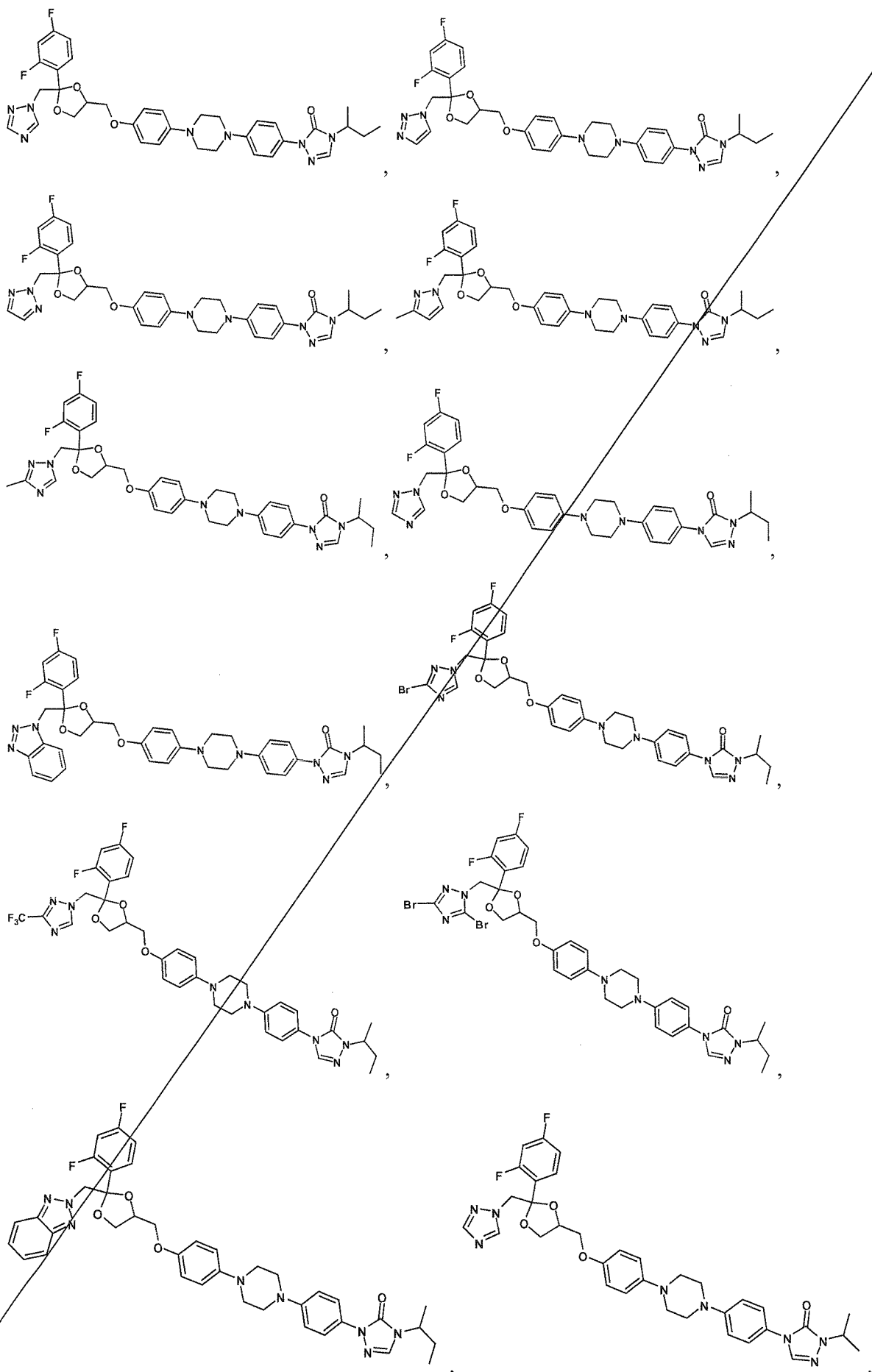
69. The compound of claim 68 wherein m is 1.

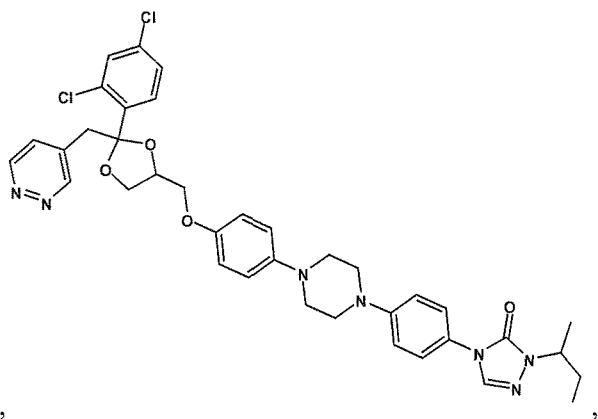
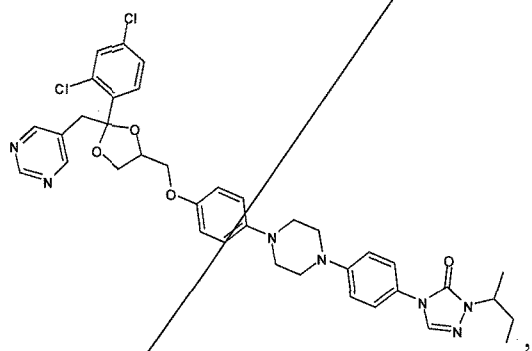
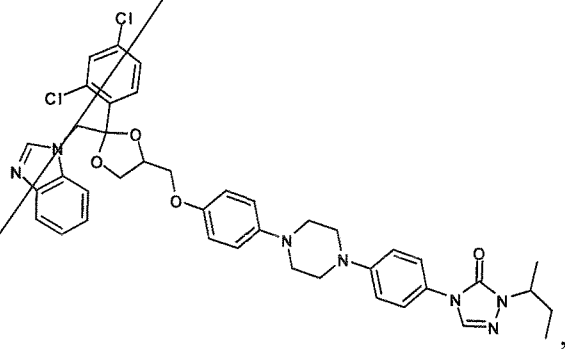
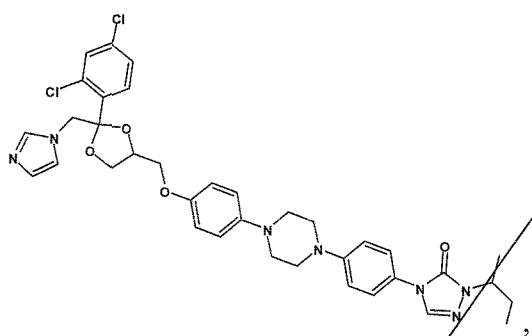
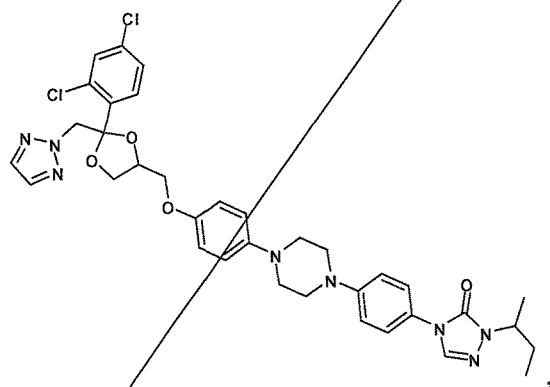
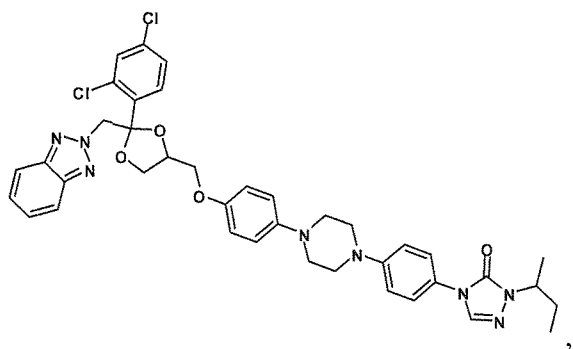
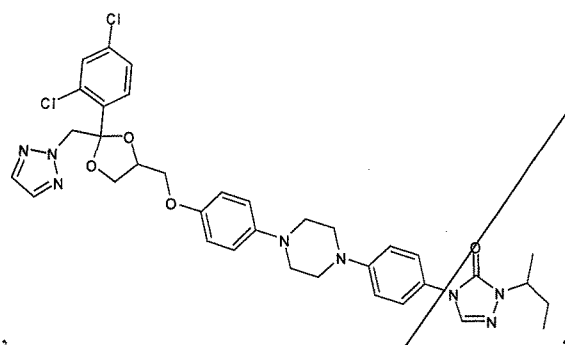
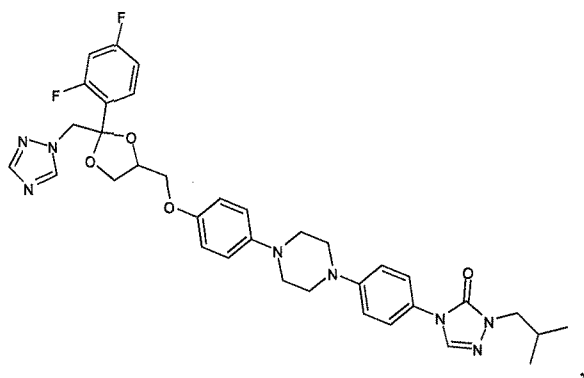
70. The compound of any one of claims 40-69 wherein p is 1, 2, or 3.

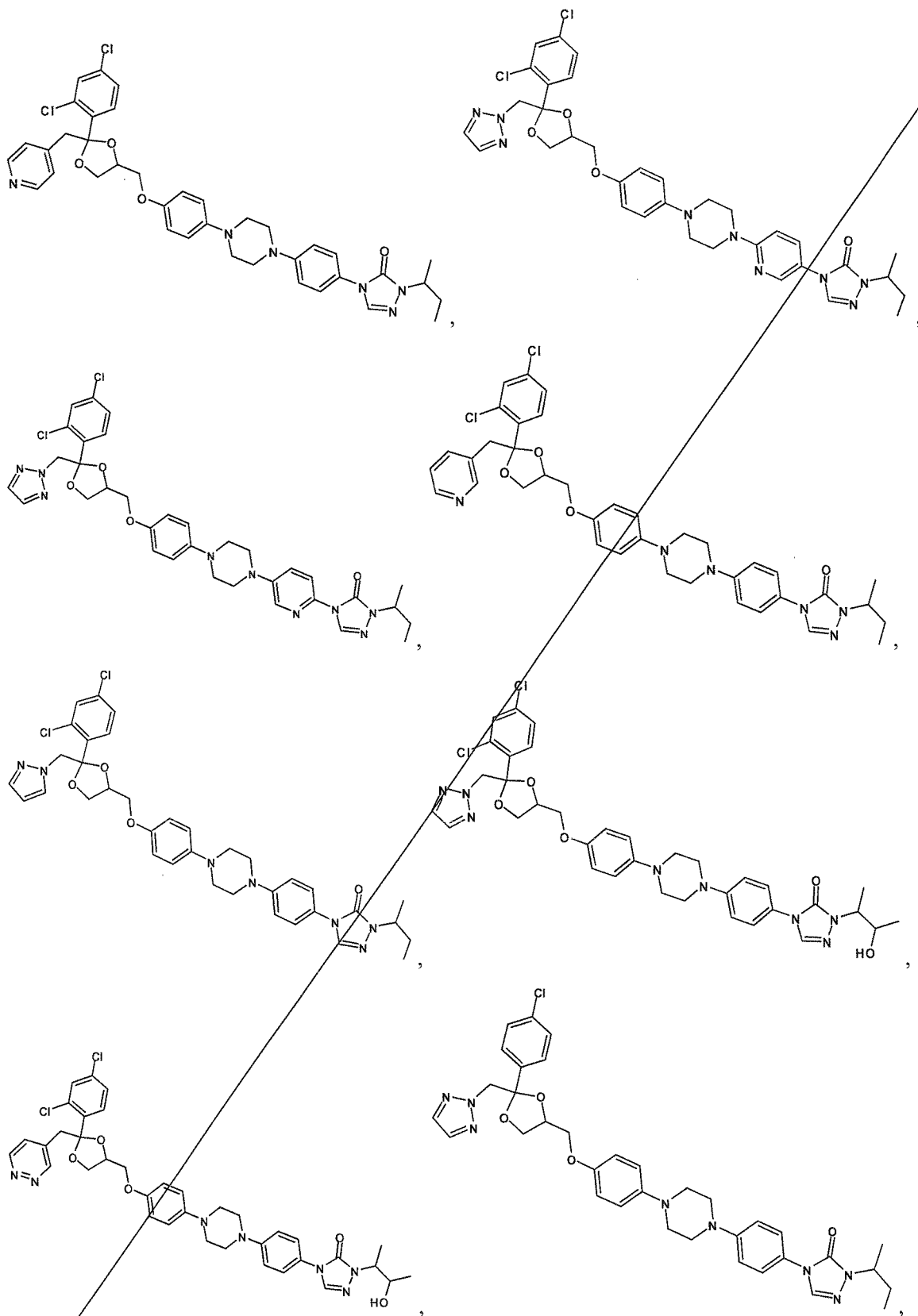
71. The compound of claim 70 wherein p is 1.

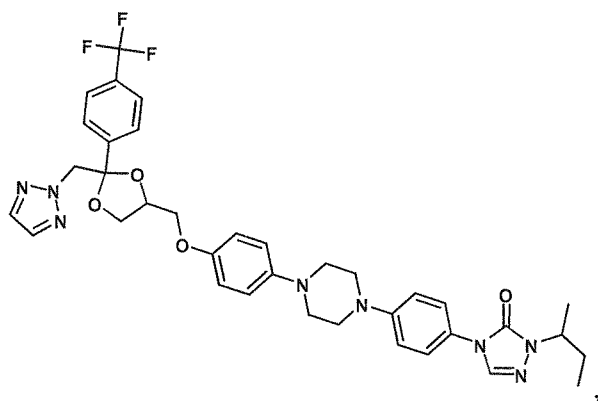
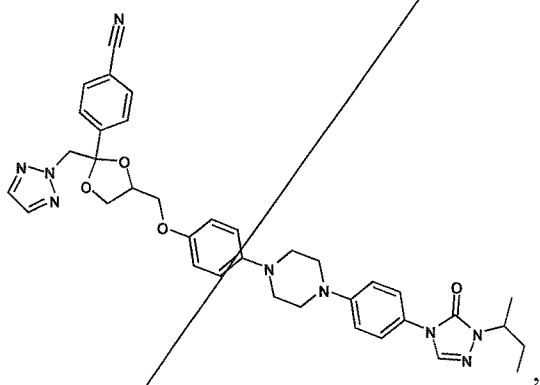
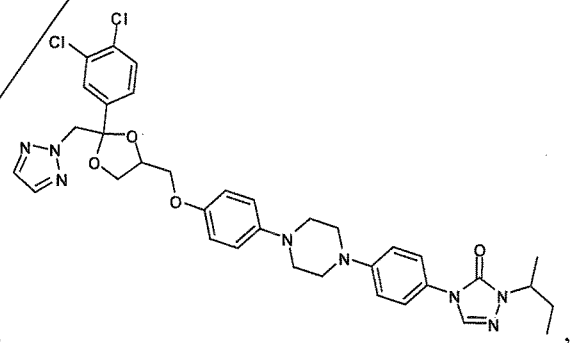
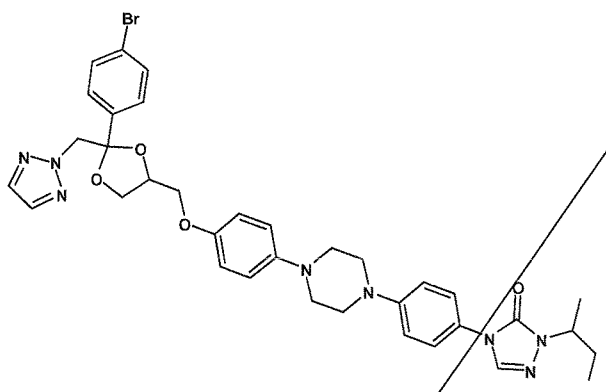
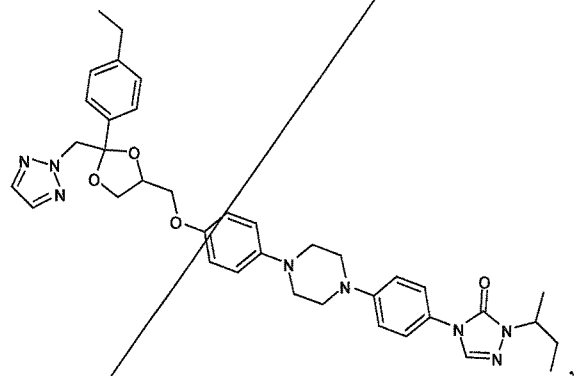
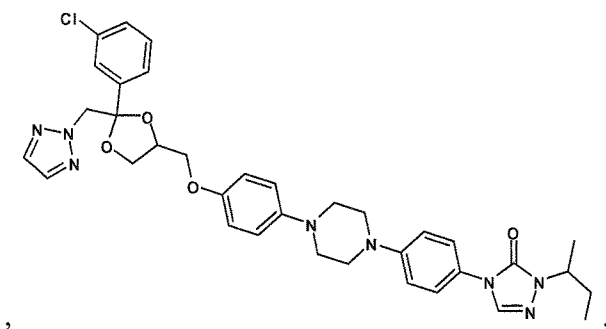
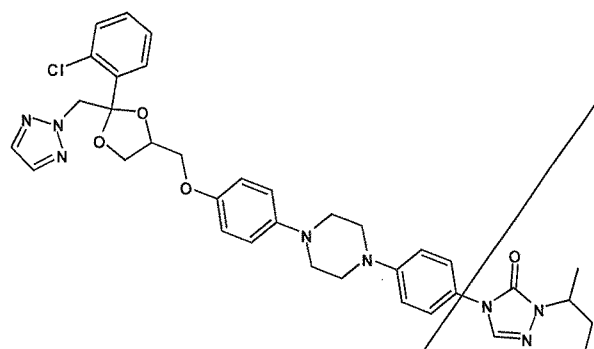
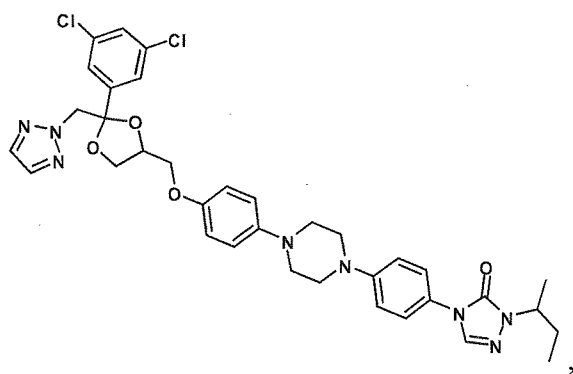
72. The compound of any one of claims 40-71 wherein R^1 , R^2 , R^3 , and R^4 are hydrogen.

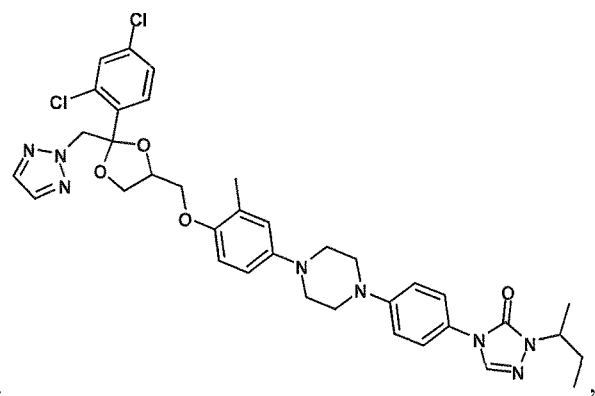
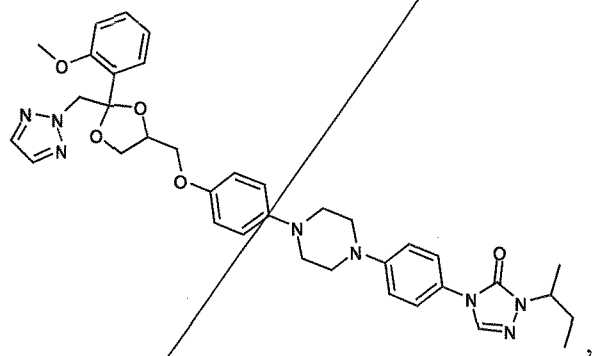
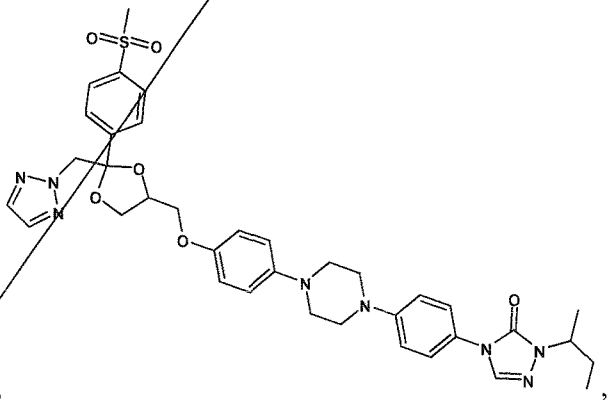
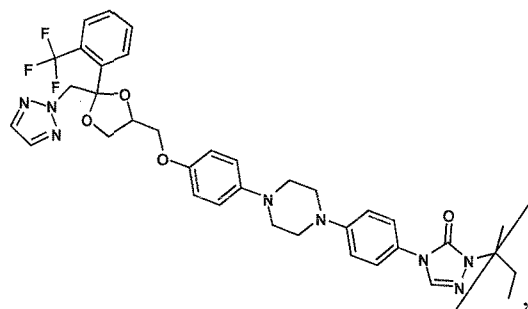
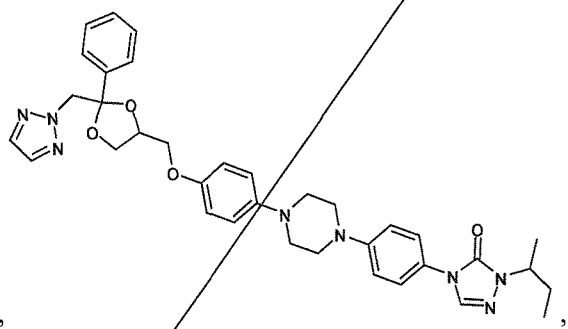
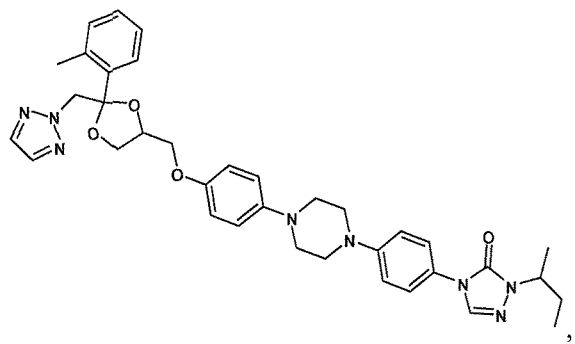
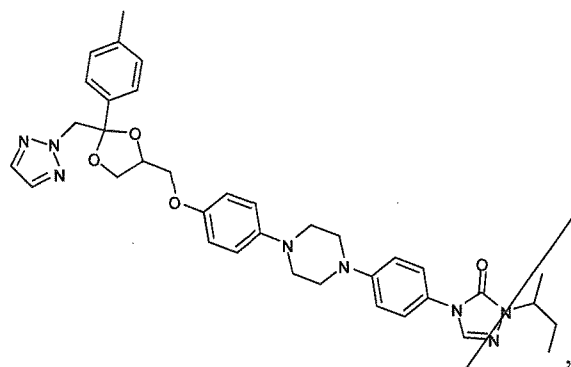
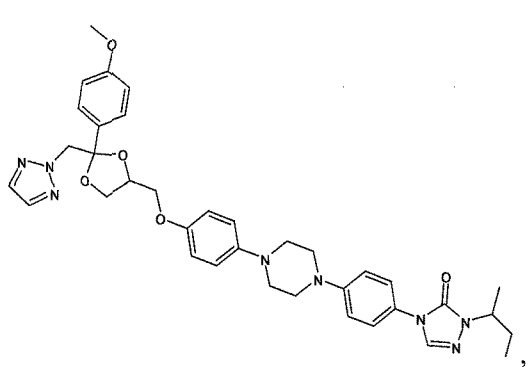
73. The compound of claim 40 wherein the compound is selected from:

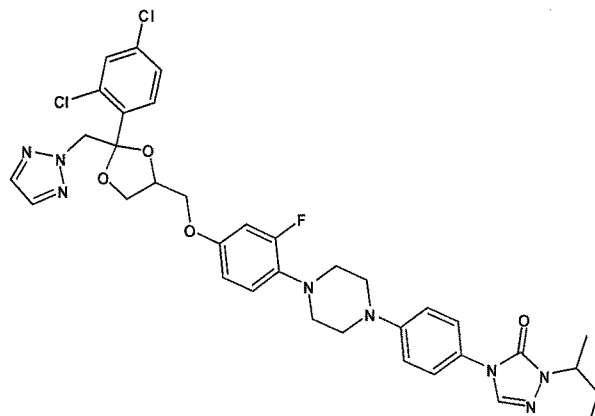
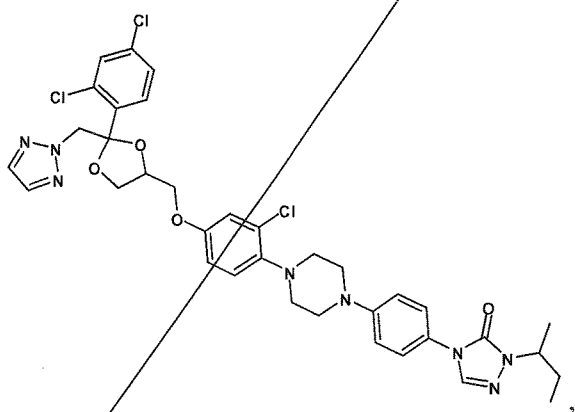
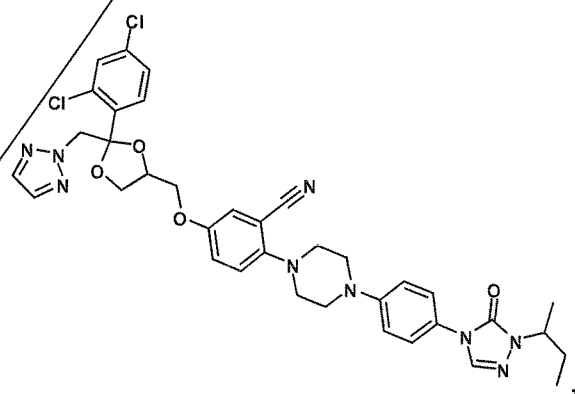
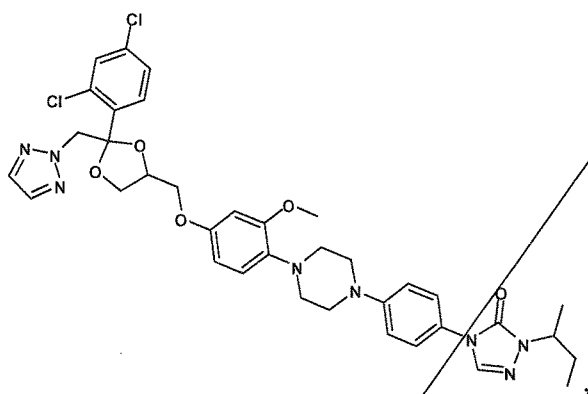
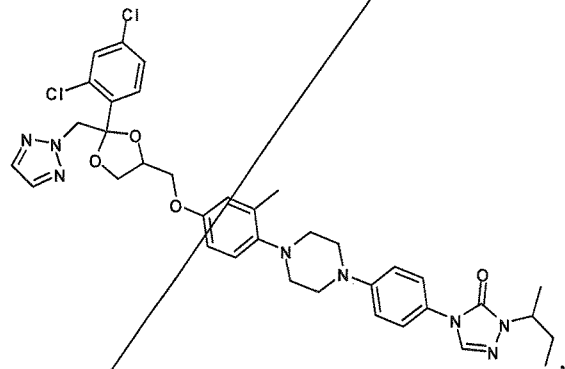
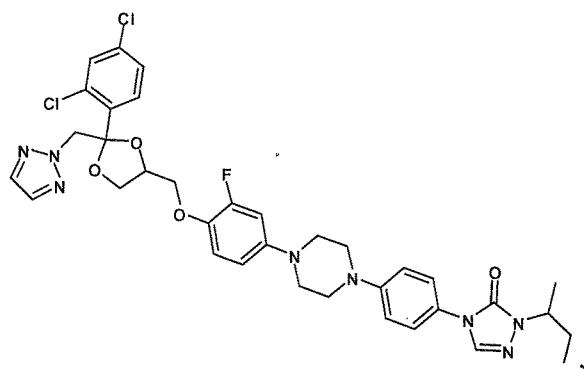
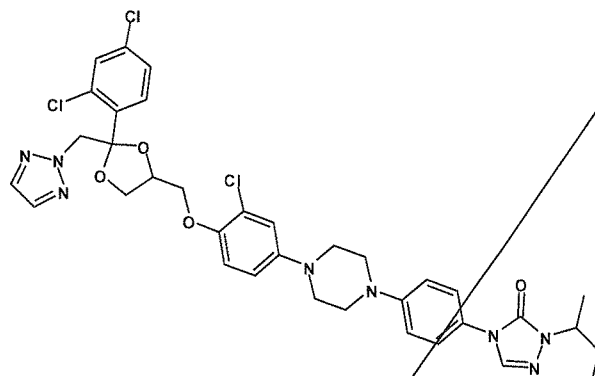
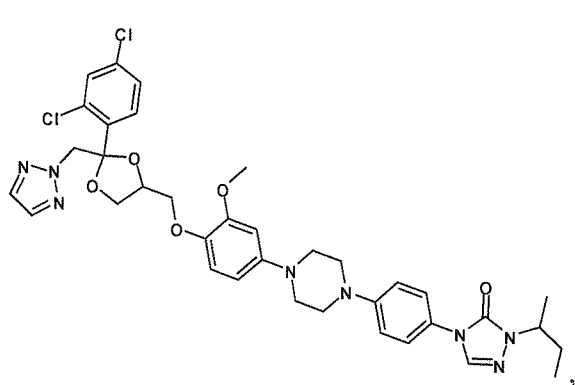


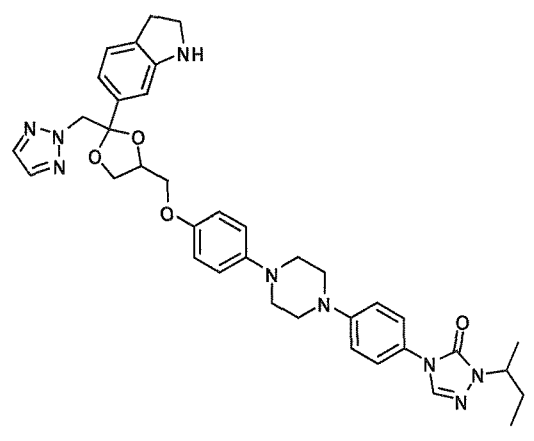
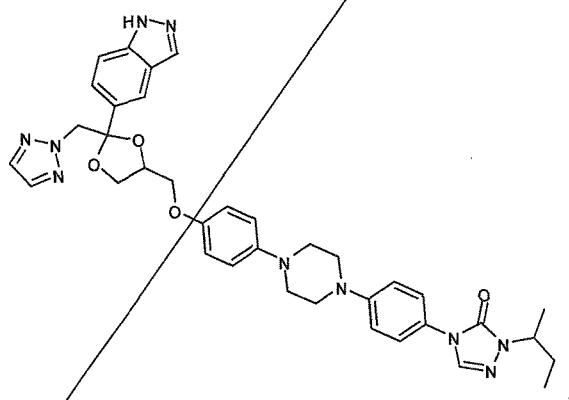
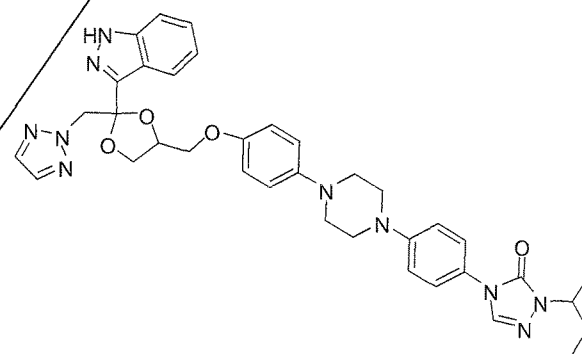
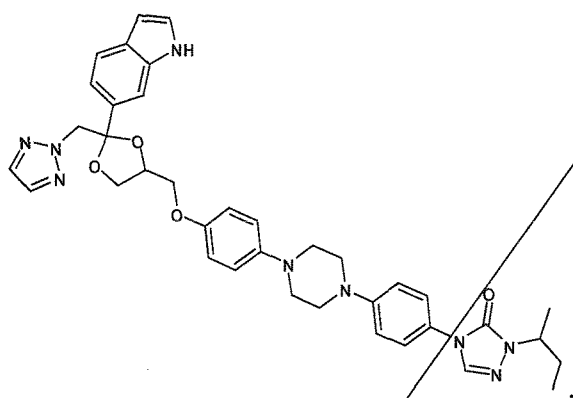
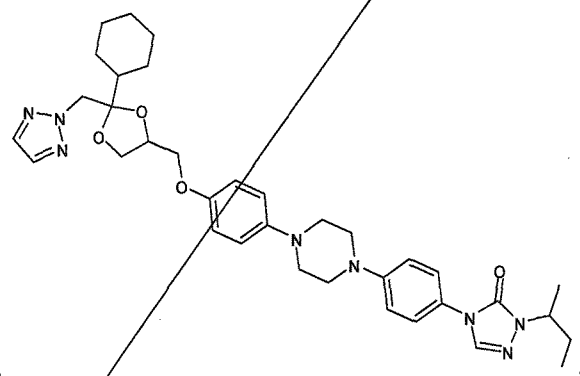
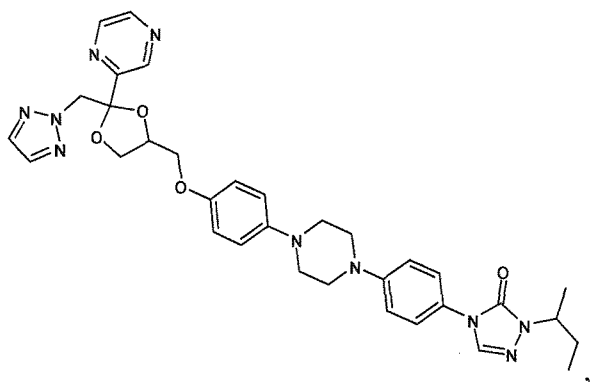
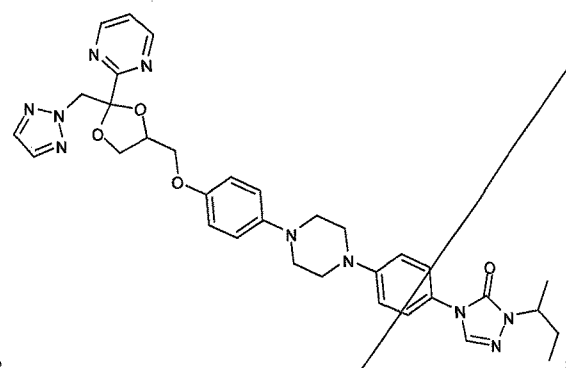
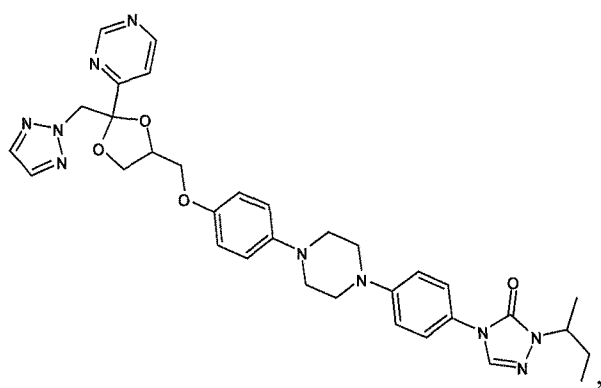


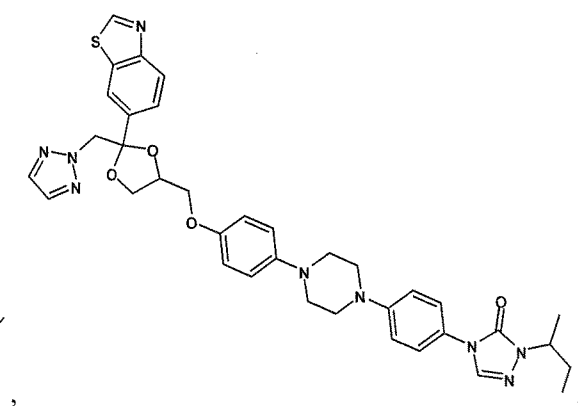
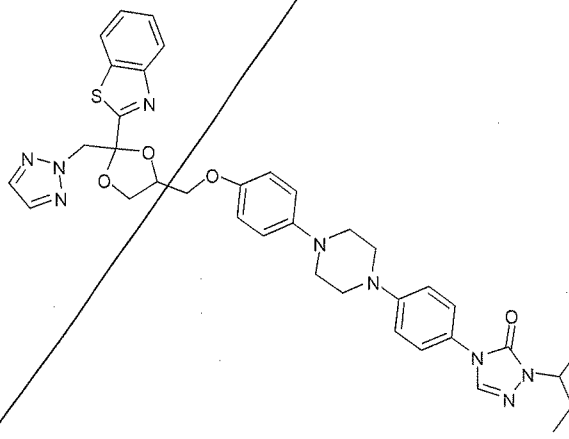
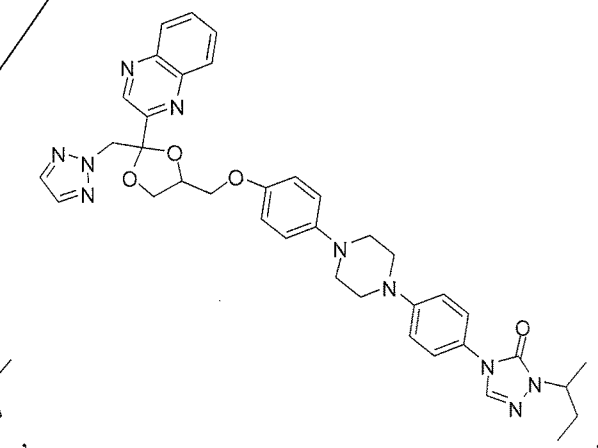
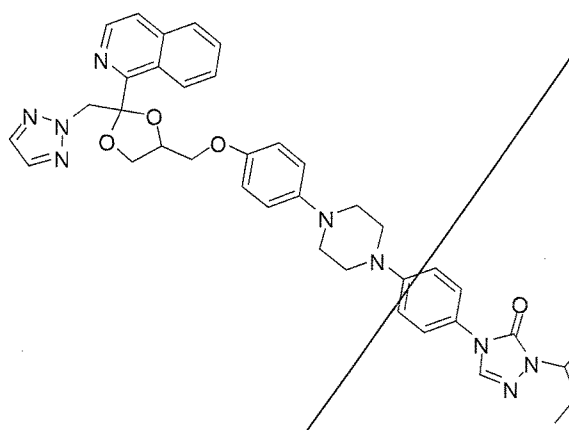
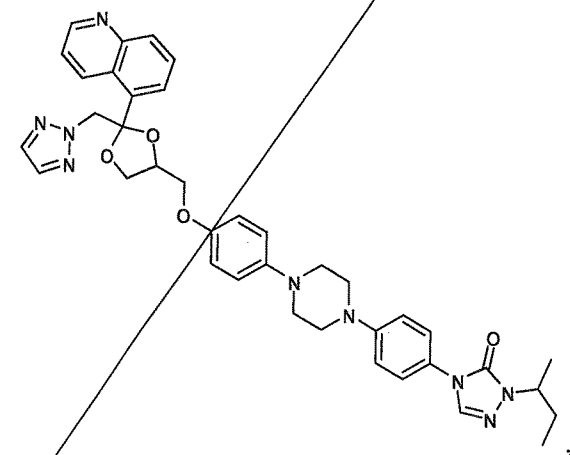
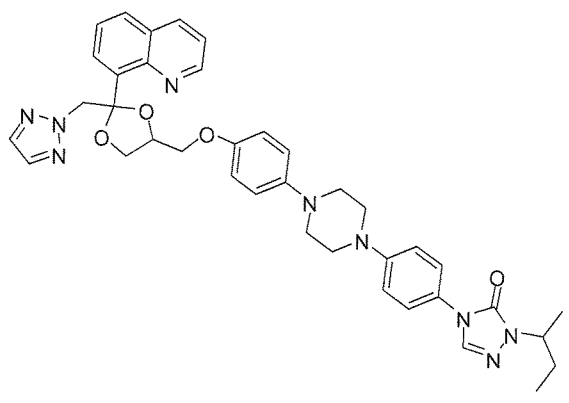
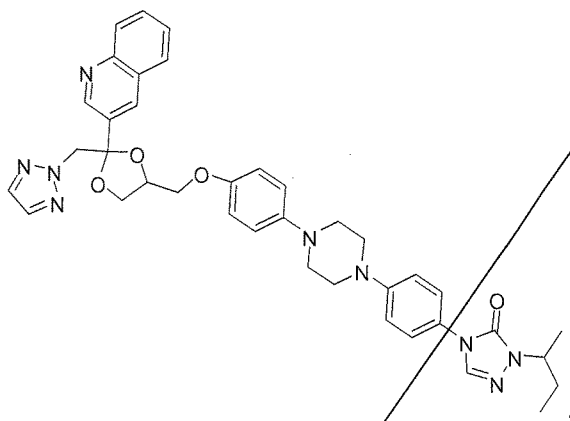
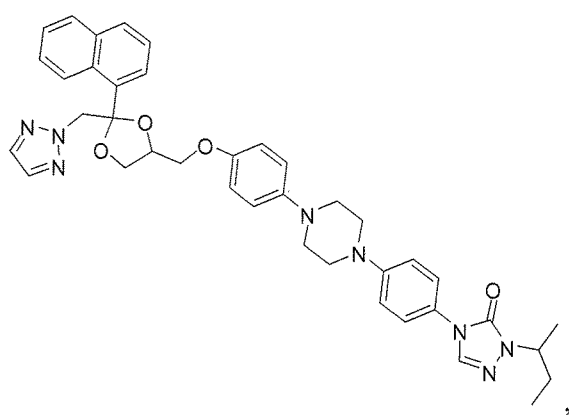


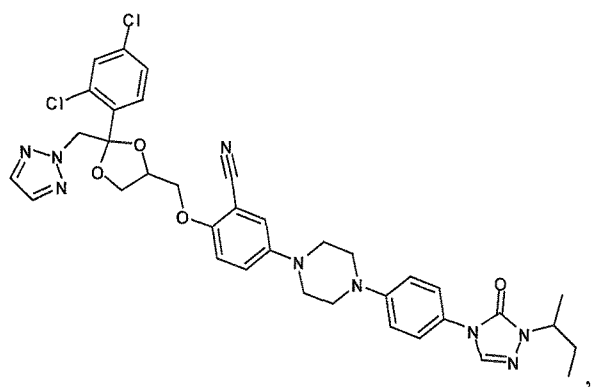
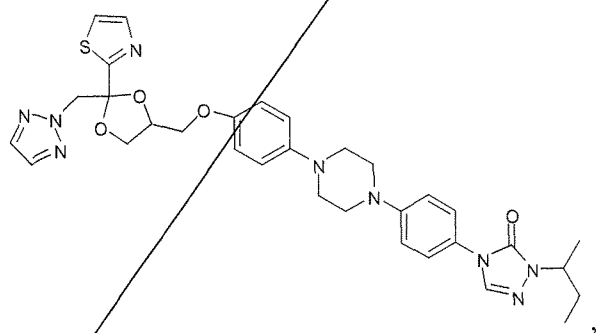
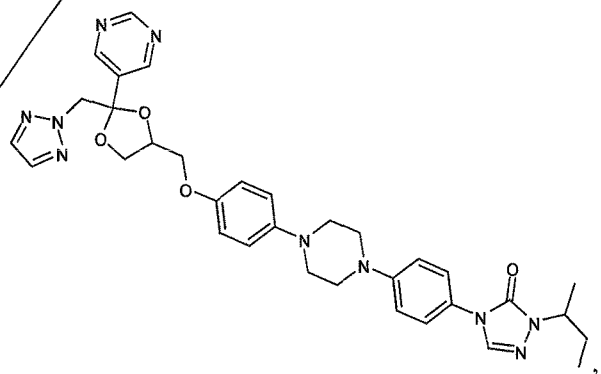
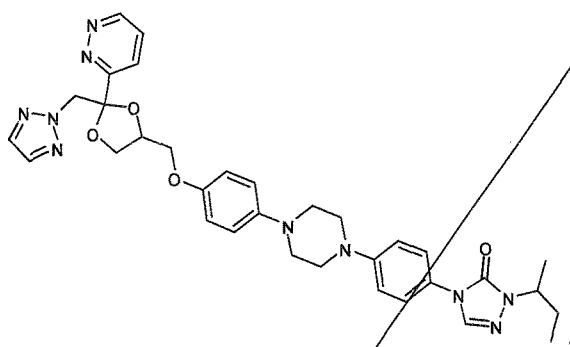
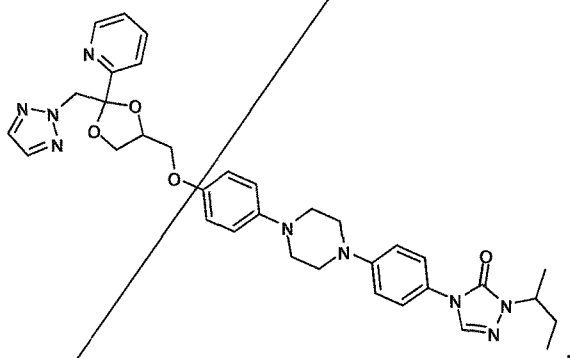
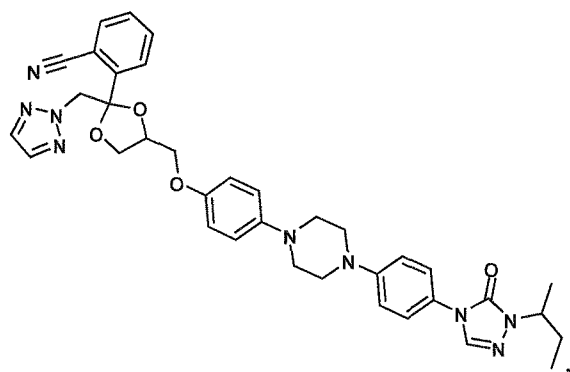
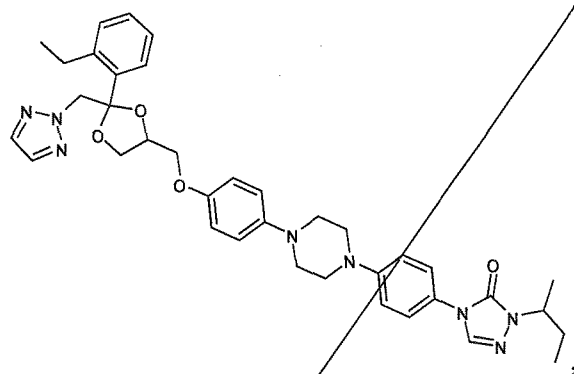
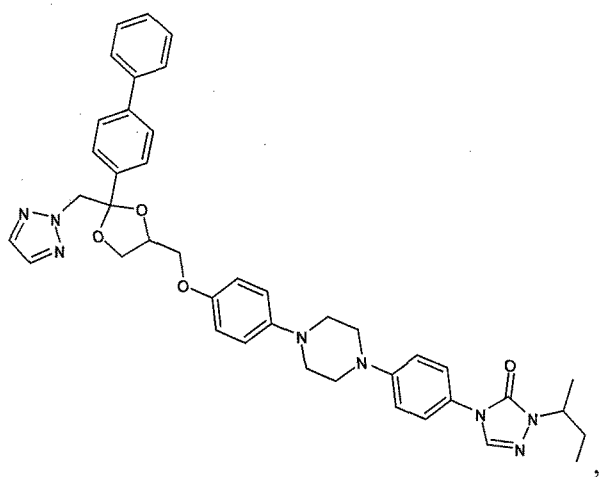


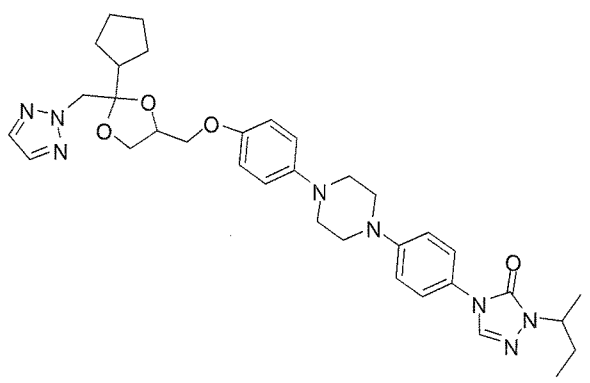
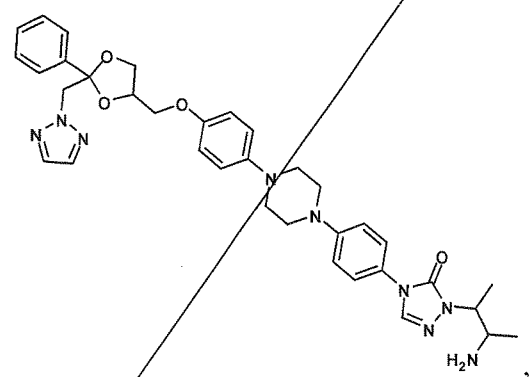
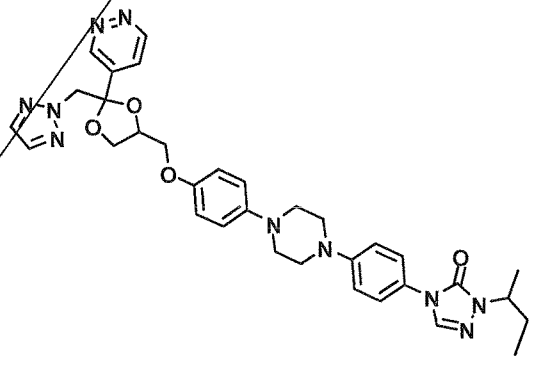
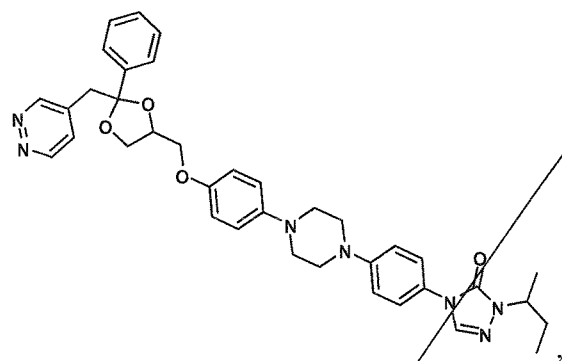
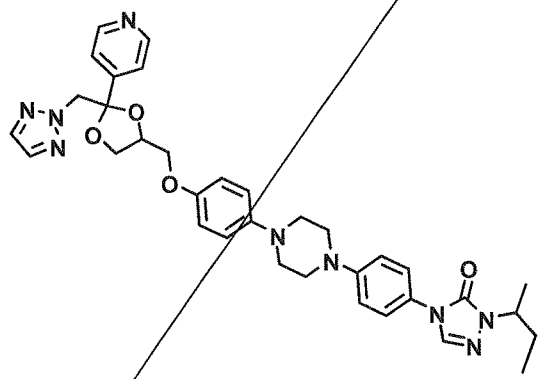
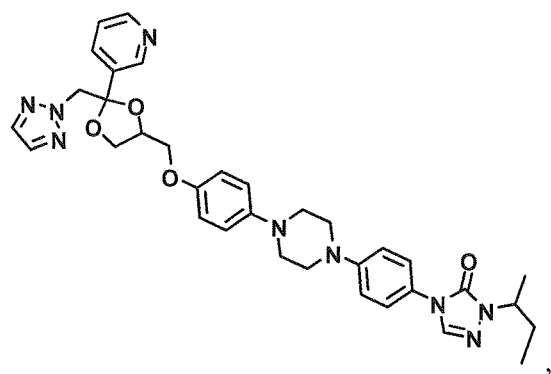
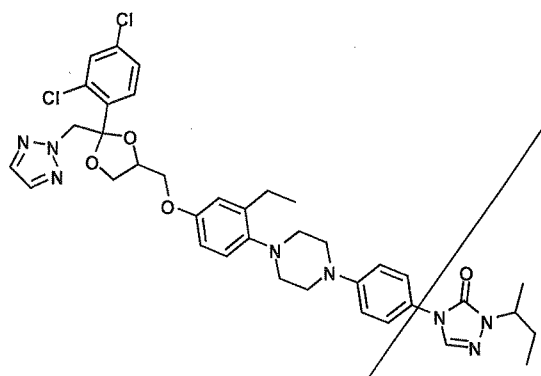
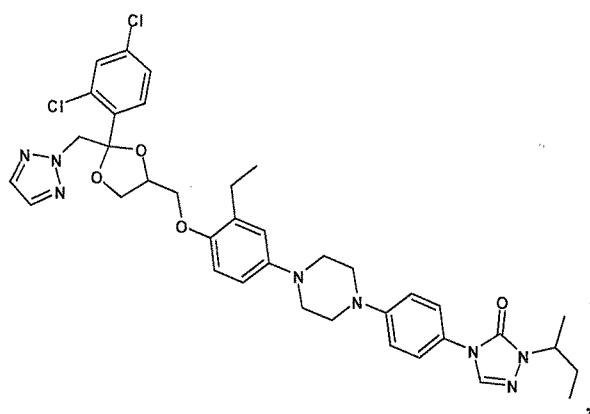


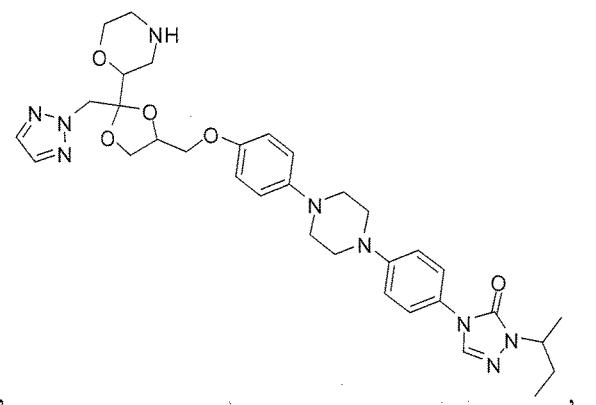
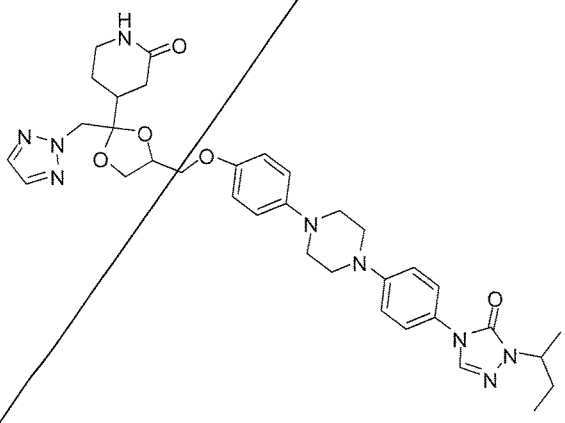
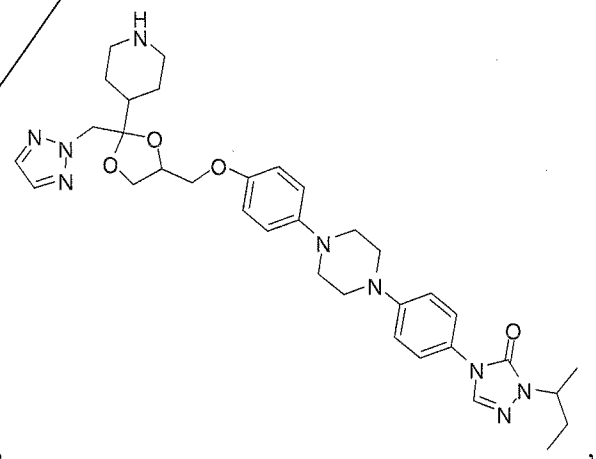
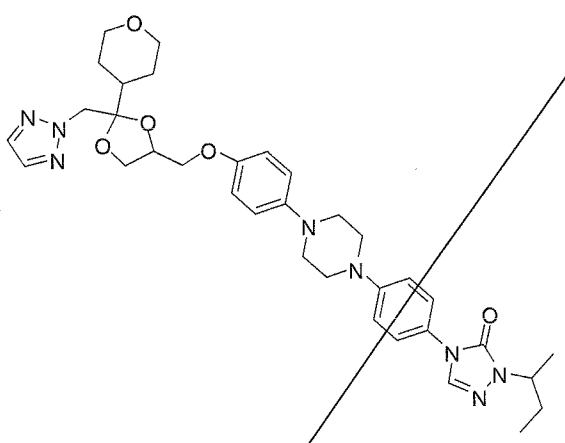
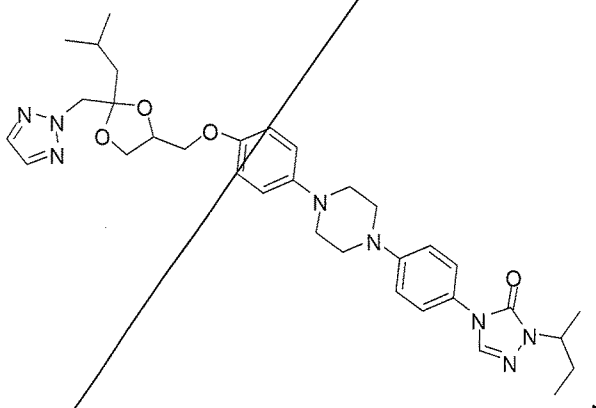
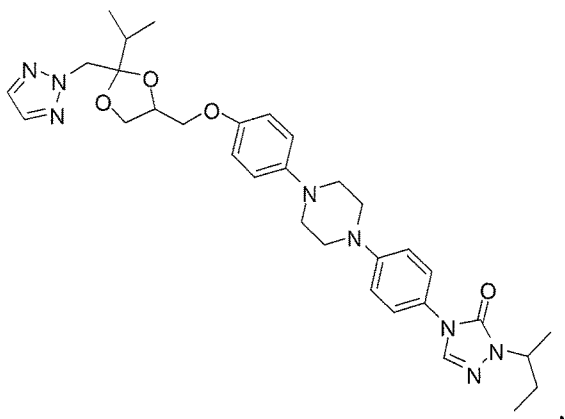
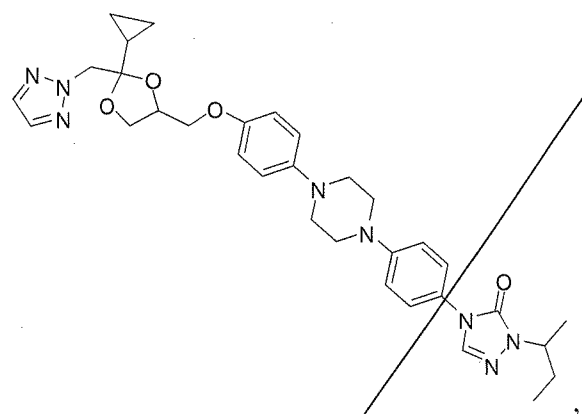
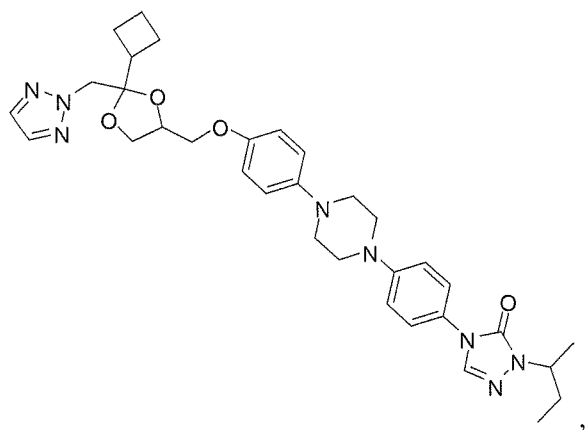


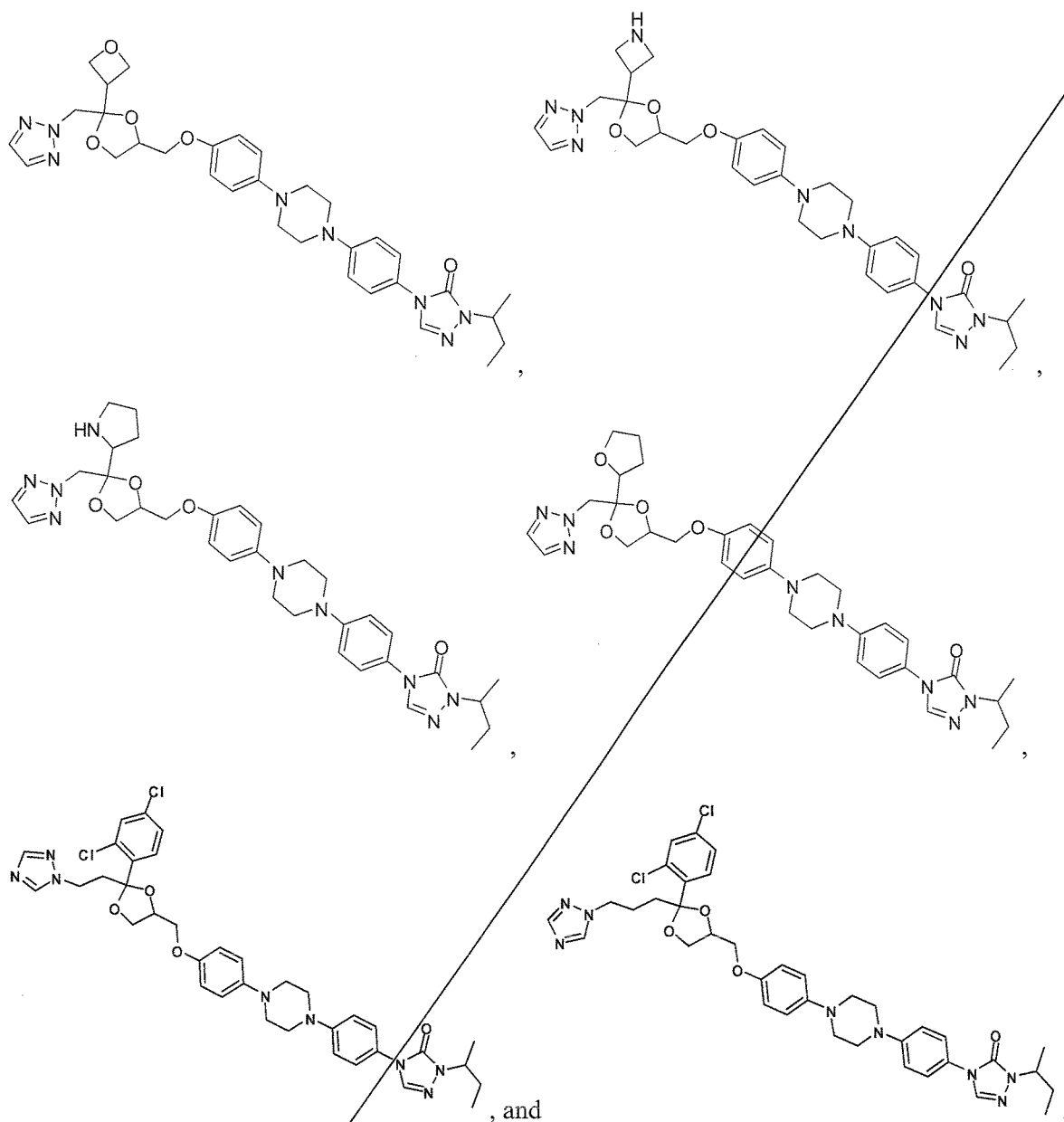








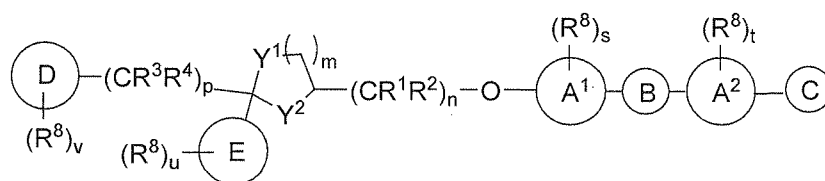




74. A pharmaceutical composition comprising a compound of any one of claims 40-73, or a pharmaceutically acceptable salt, solvate, polymorph, prodrug, metabolite, N-oxide, stereoisomer, or isomer thereof, and a pharmaceutically acceptable excipient.

CLAIMS

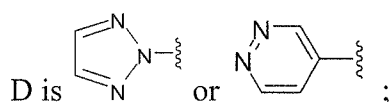
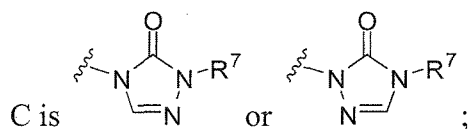
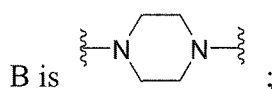
1. Use of a therapeutically effective amount of a compound of Formula (I), a pharmaceutically acceptable salt, solvate, stereoisomer, or isomer thereof:



Formula (I)

wherein:

A^1 and A^2 are independently selected from aryl or heteroaryl;



E is aryl, heteroaryl, carbocyclyl, or heterocyclyl;

each R^1 , R^2 , R^3 , and R^4 is H;

R^7 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene($NR^{13}R^{14}$), cycloalkyl, heterocyclyl, -alkylene(cycloalkyl), or -alkylene(heterocyclyl);

each R^8 is independently selected from alkyl, cycloalkyl, heterocyclyl, halo, hydroxy, nitrile, azido, nitro, alkoxy, haloalkoxy, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene($NR^{13}R^{14}$), -alkylene(cycloalkyl), -alkylene(heterocyclyl), aryl, heteroaryl, - SR^{13} , - SOR^{13} , - SO_2R^{13} , - $SO_2NR^{13}R^{14}$, - $NR^{13}R^{14}$, - $NR^{13}SO_2R^{14}$, - $NR^{13}C(O)R^{14}$, - $NR^{13}C(O)OR^{14}$, - $NR^{13}C(O)NR^{13}R^{14}$, - $C(O)R^{14}$, - $C(O)OR^{14}$, and - $C(O)NR^{13}R^{14}$; or two adjacent R^8 form a heterocyclyl ring;

each R^{13} and R^{14} is independently selected from H, alkyl, cycloalkyl, heterocyclylalkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, arylalkyl, heteroarylalkyl, aryl, and heteroaryl; or R^{13} and R^{14} taken together form a heterocycle with the atoms to which they are attached;

Y^1 and Y^2 are O;

n is 1, 2, or 3;

m is 1;

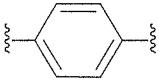
p is 1, 2, 3, or 4;

s is 0, 1, 2, 3, or 4;

t is 0, 1, 2, 3, or 4;

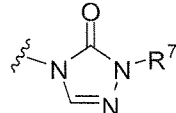
u is 0, 1, 2, 3, 4 or 5; and

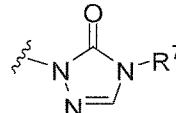
v is 0, 1, 2, 3, or 4, in the manufacture of a medicament for treating fibrosis, a disorder characterized by fibrosis, or a disease characterized by fibrosis.

2. The use of claim 1 wherein A¹ is .

3. The use of claim 1 or 2, wherein A² is .

4. The use of claim 1 or 2, wherein A² is pyridine, pyrazine, pyrimidine, pyridazine, or triazine.

5. The use of any one of claims 1-4, wherein C is ; and R⁷ is alkyl.

6. The use of any one of claims 1-4, wherein C is ; and R⁷ is alkyl.

7. The use of any one of claims 1-6, wherein E is cycloalkyl.

8. The use of claim 7, wherein E is cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

9. The use of any one of claims 1-6, wherein E is heterocyclyl.

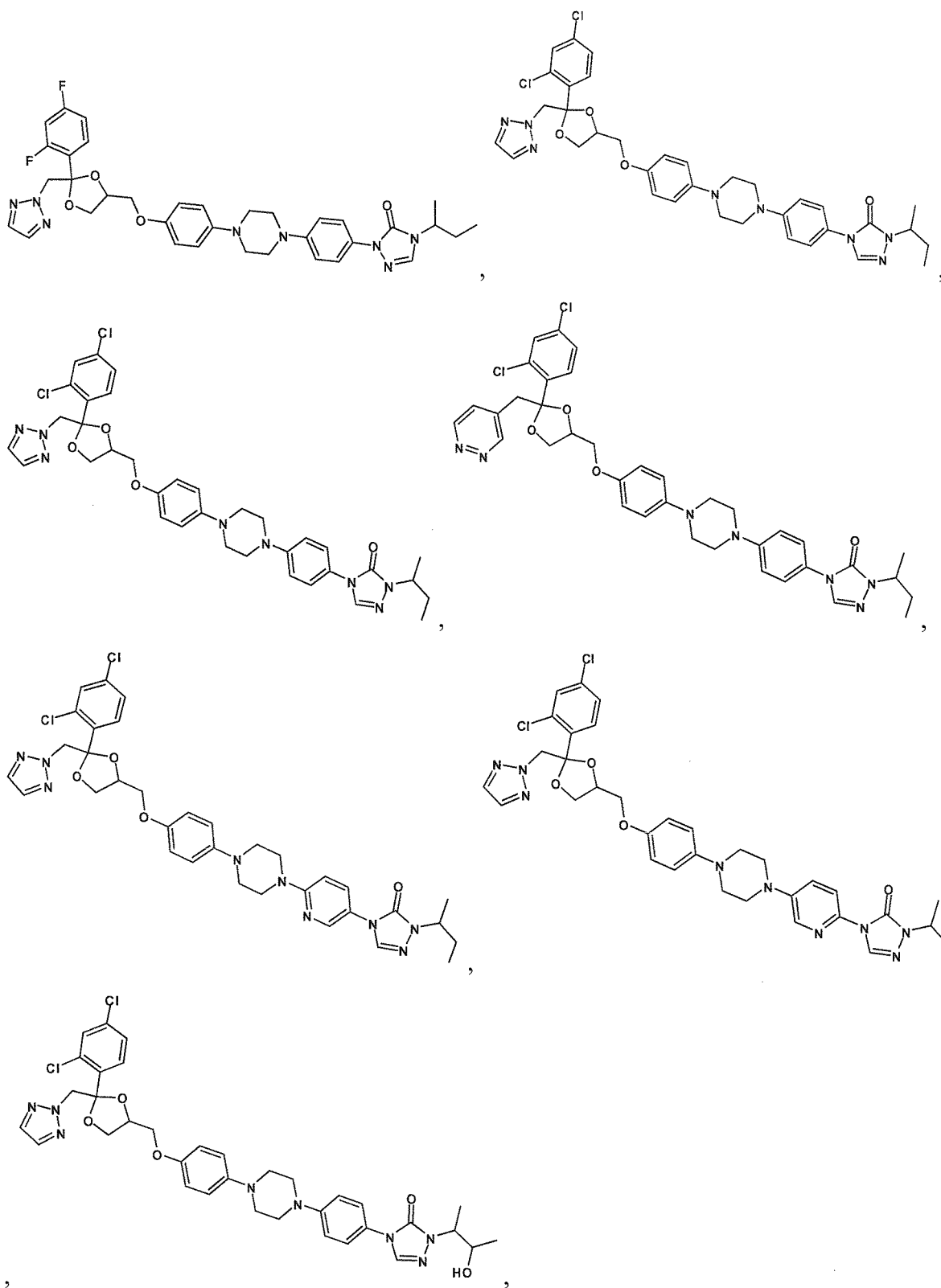
10. The use of any one of claims 1-6, wherein E is .

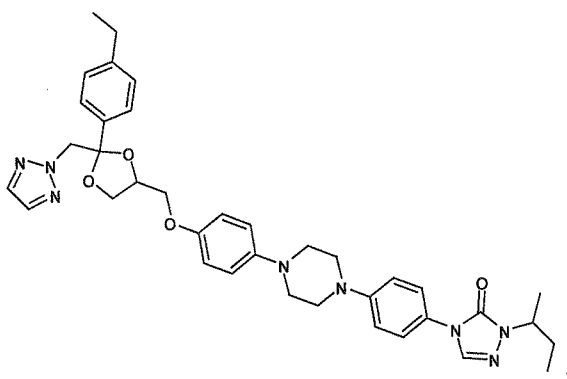
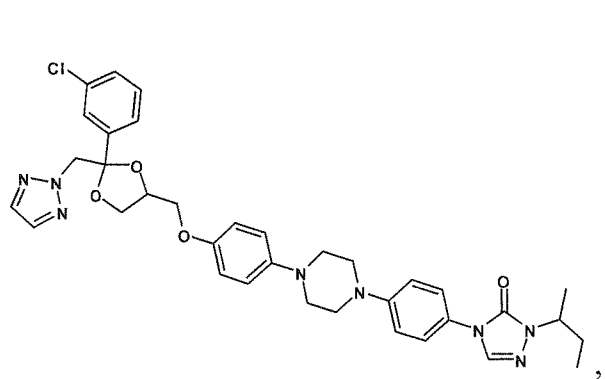
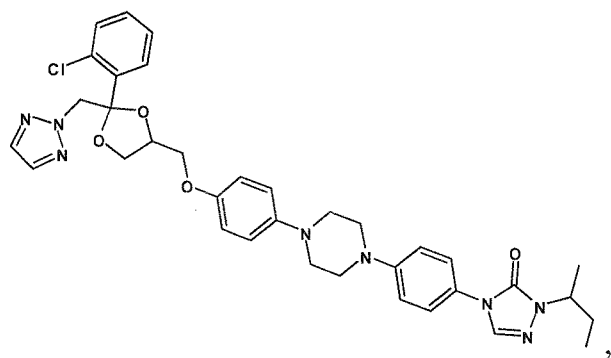
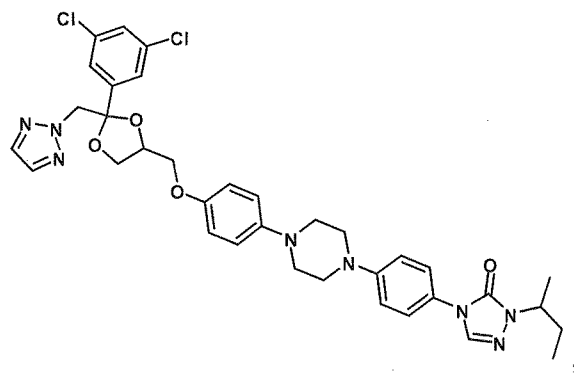
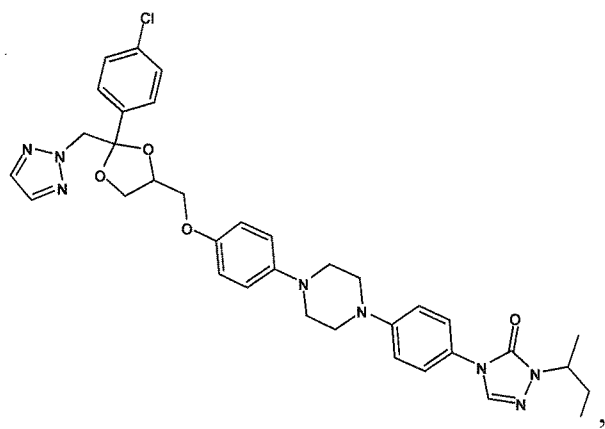
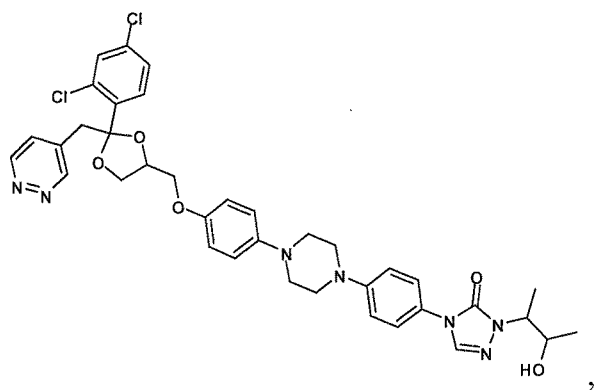
11. The use of any one of claims 1-6, wherein E is heteroaryl.

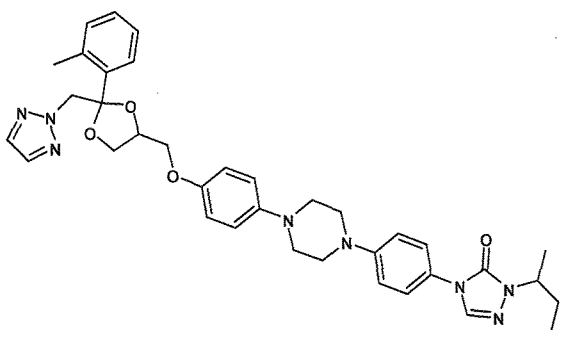
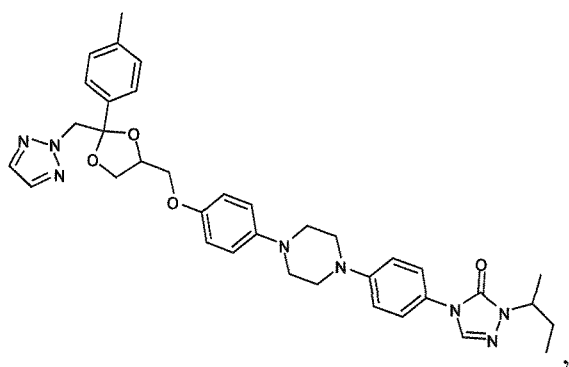
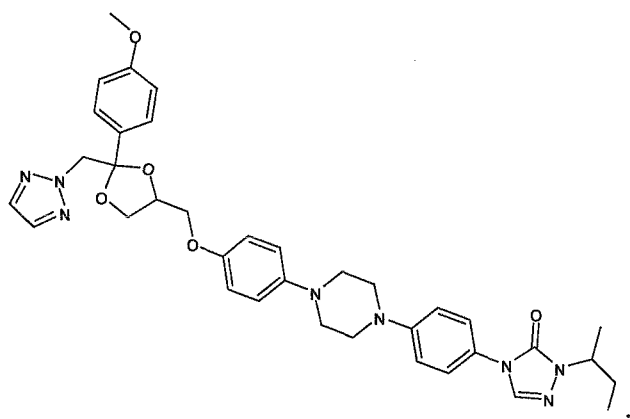
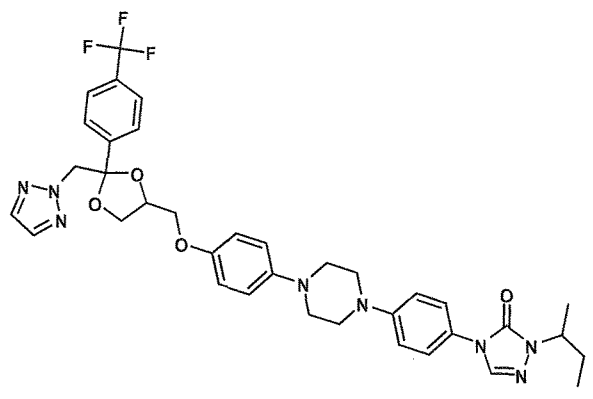
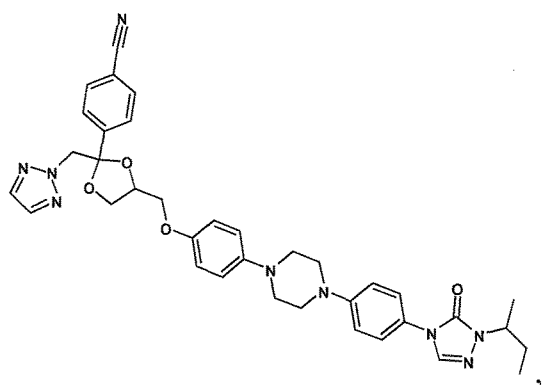
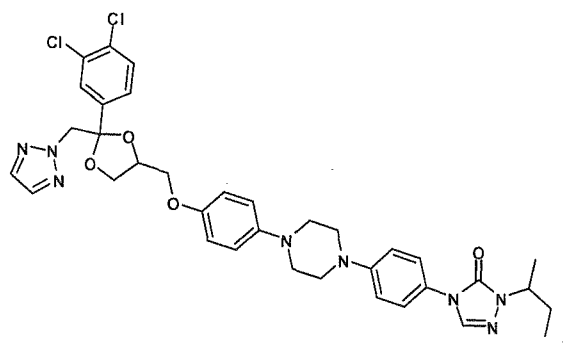
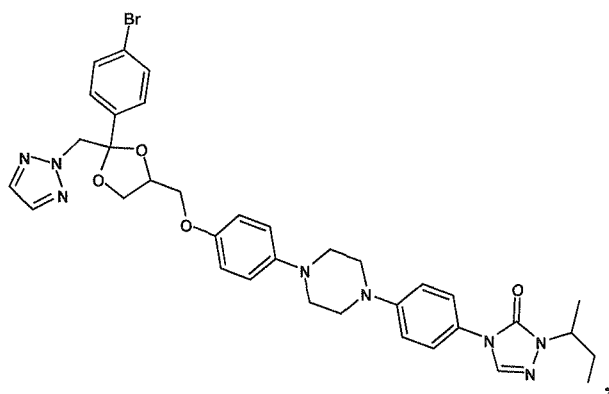
12. The use of any one of claims 1-11, wherein p is 1, 2, or 3.

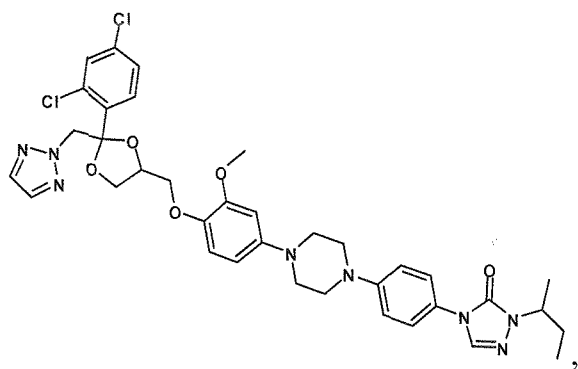
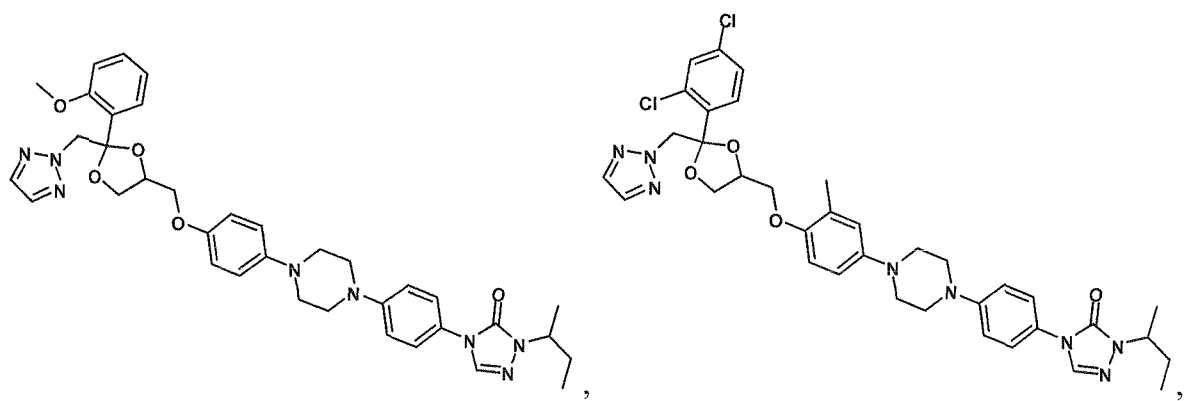
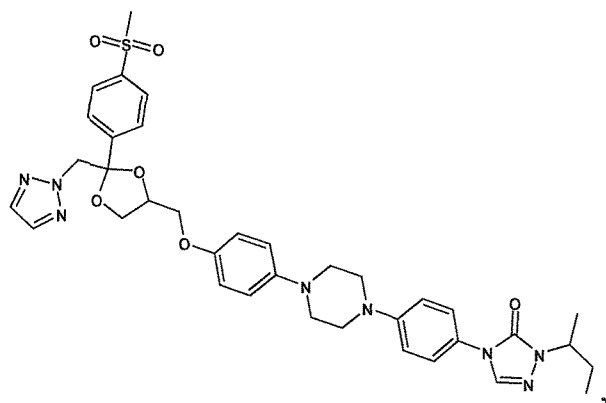
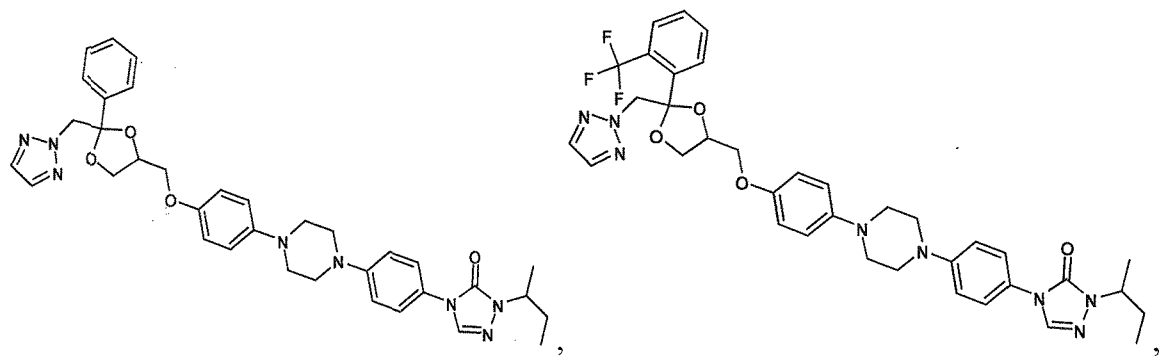
13. The use of claim 12, wherein p is 1.

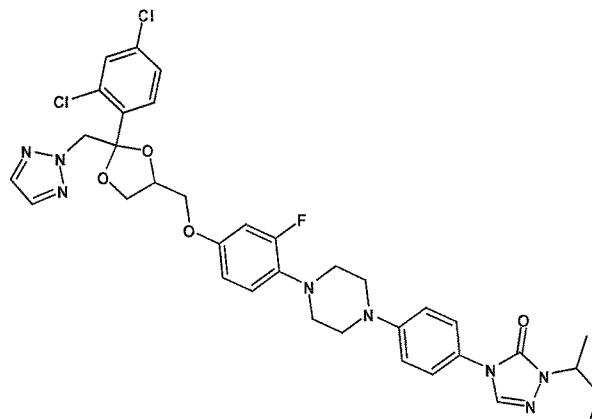
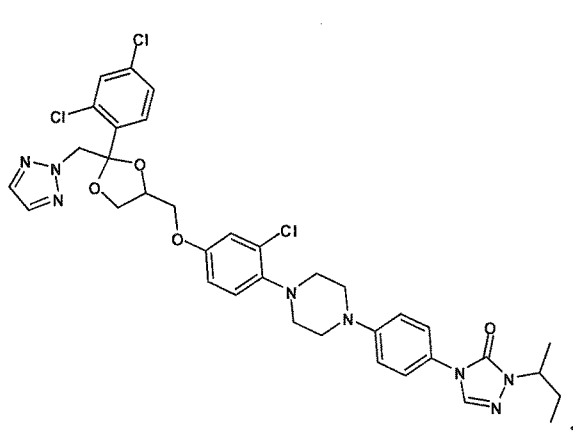
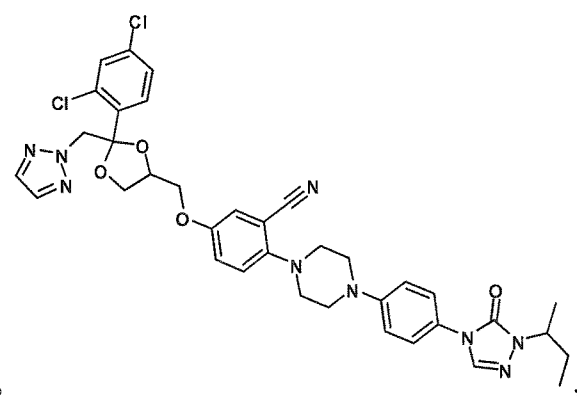
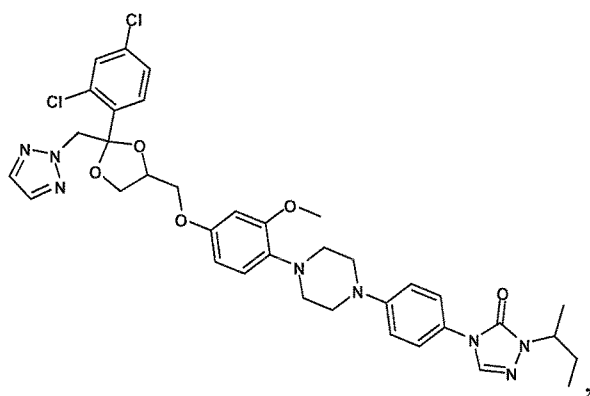
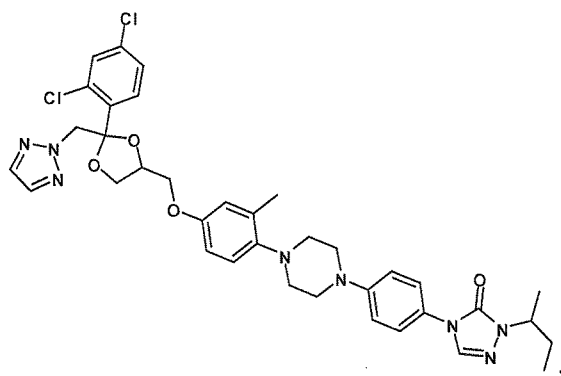
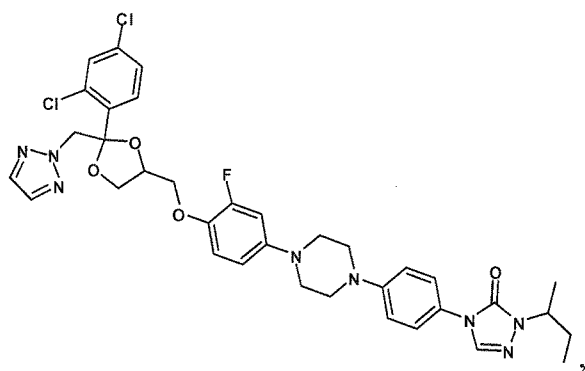
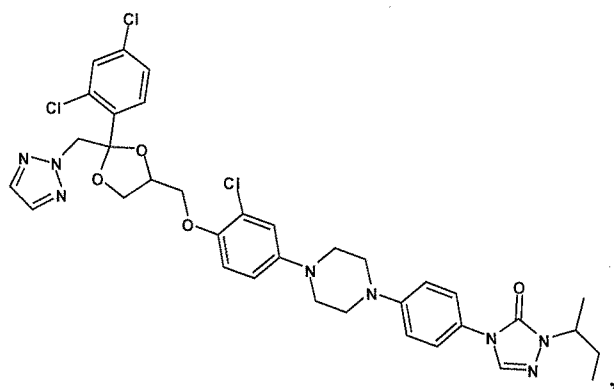
14. The use of claim 1, wherein the compound is selected from:

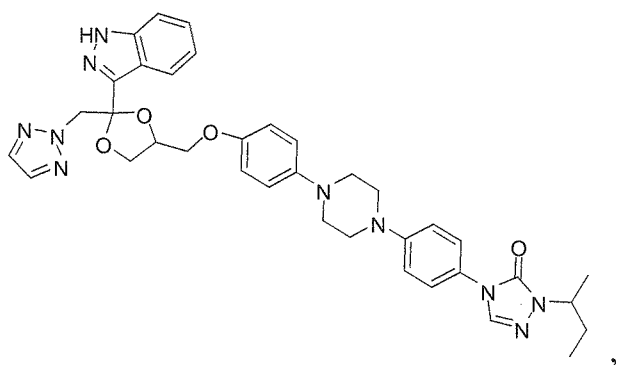
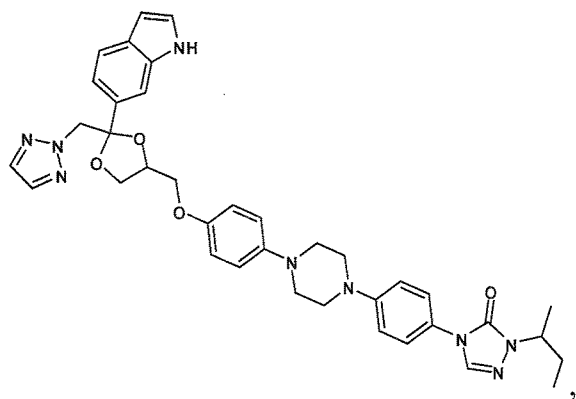
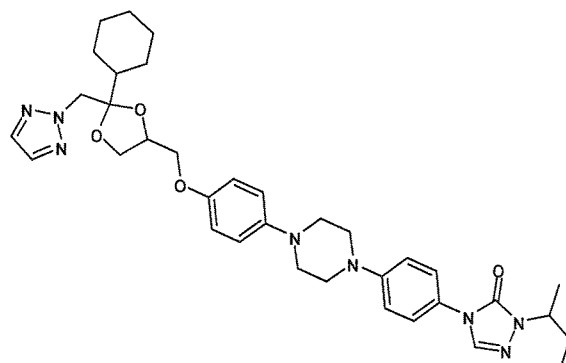
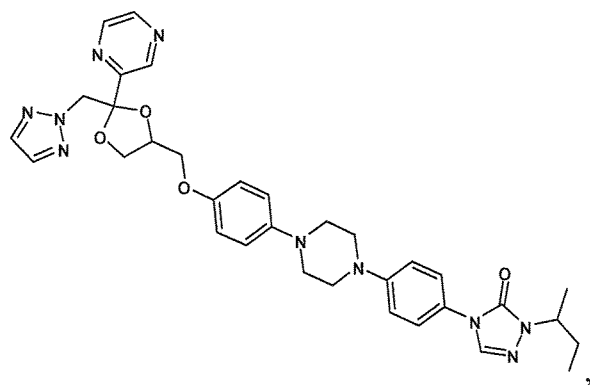
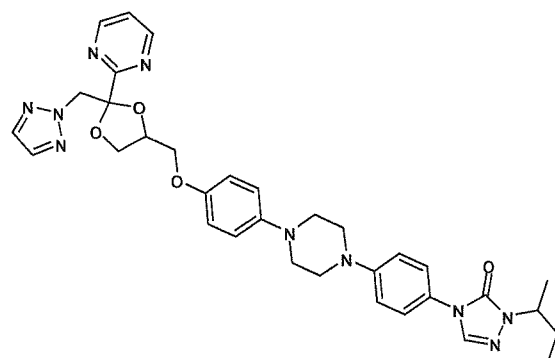
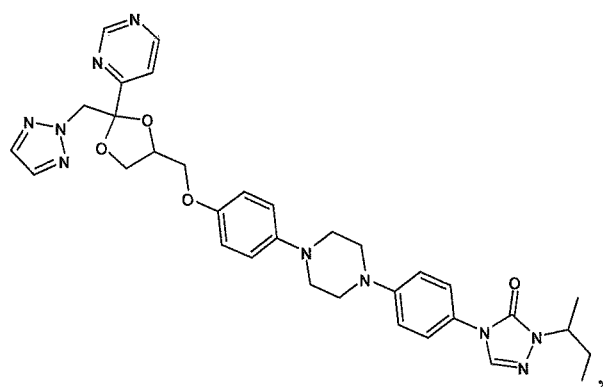


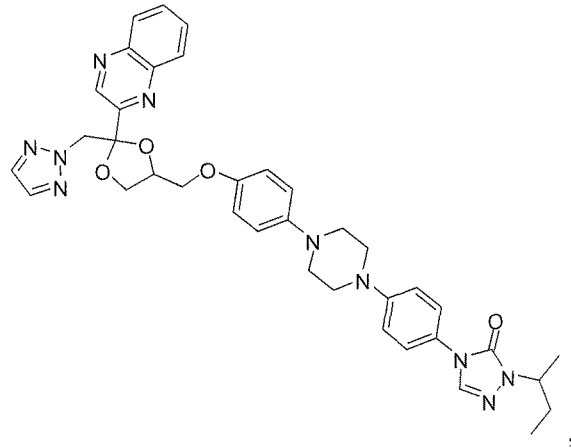
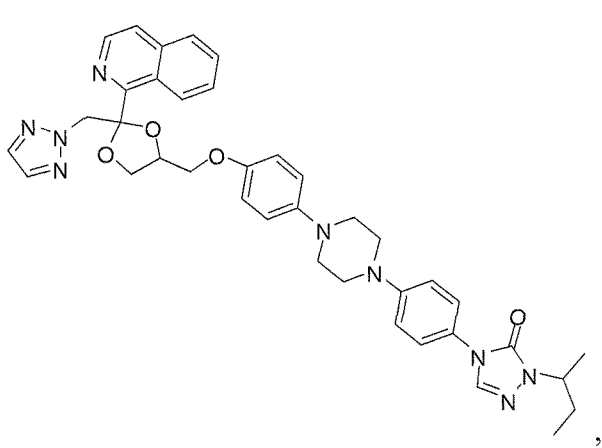
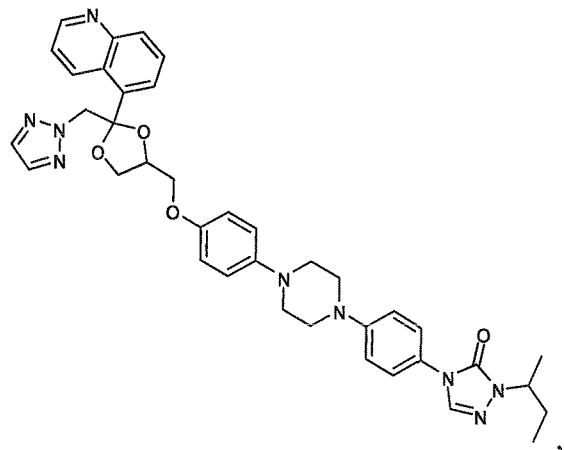
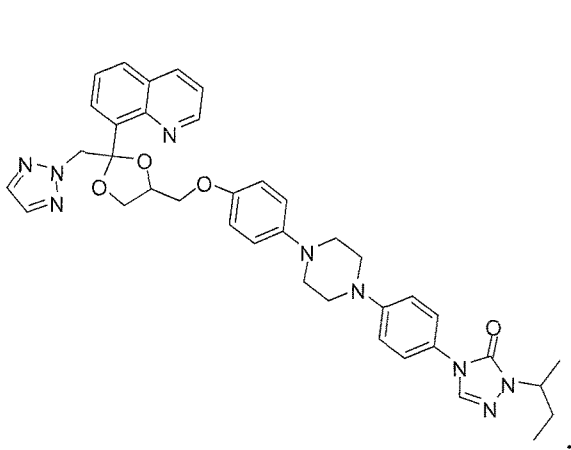
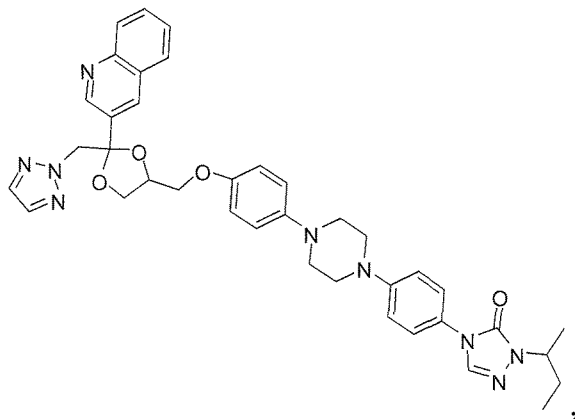
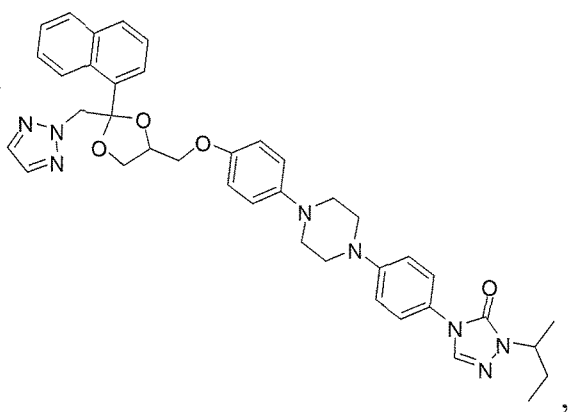
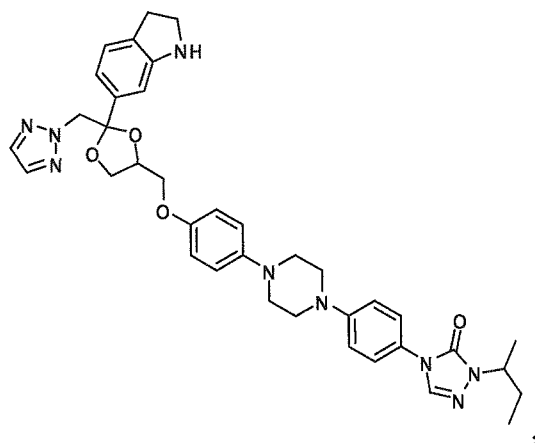
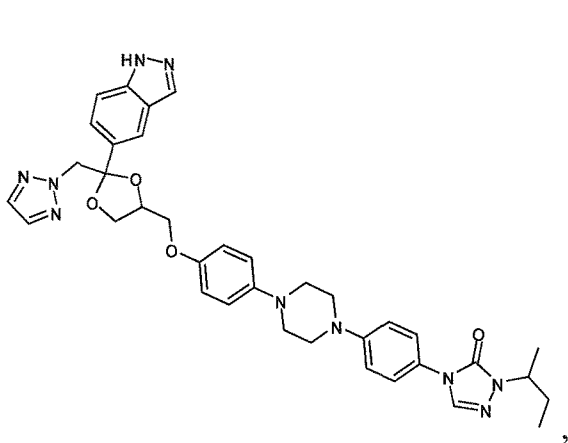


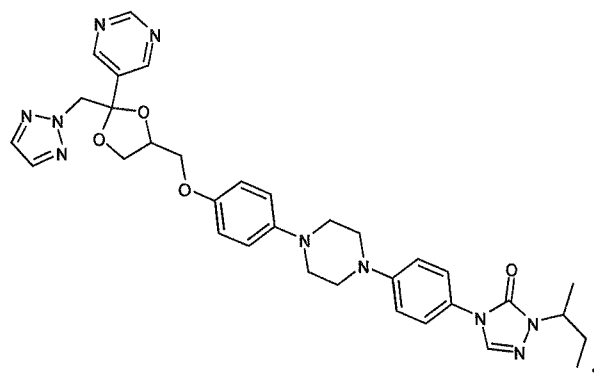
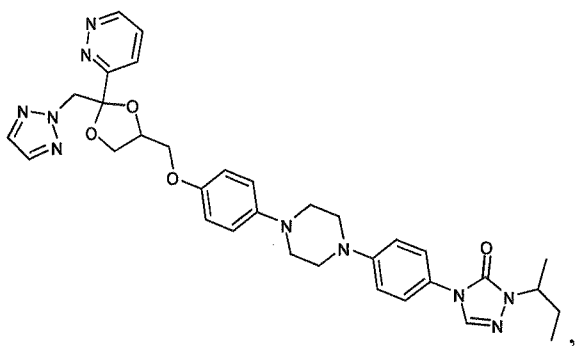
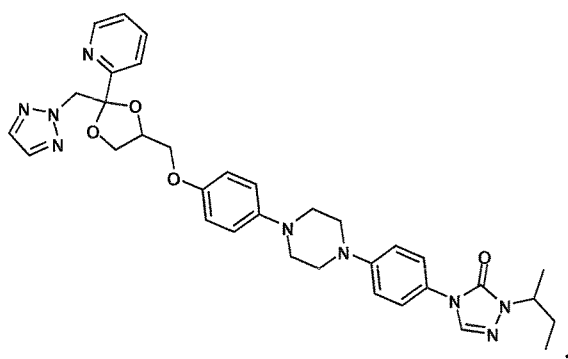
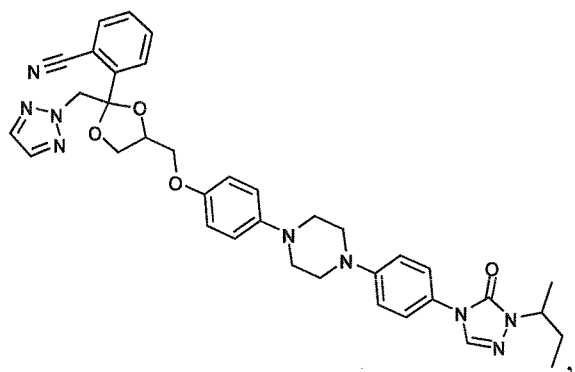
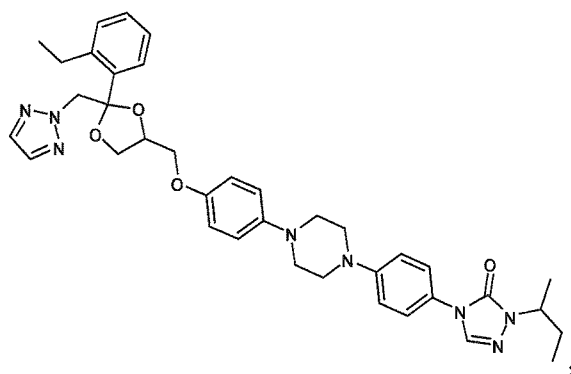
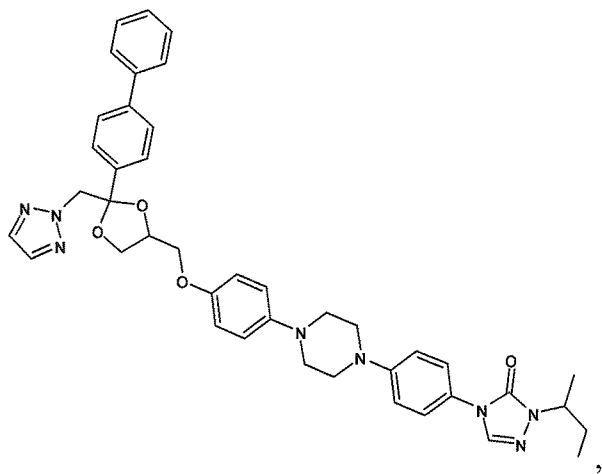
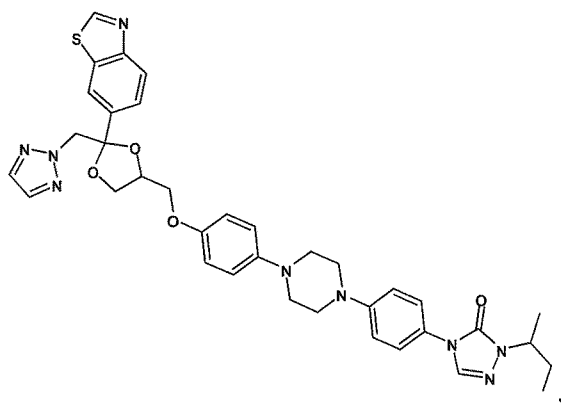
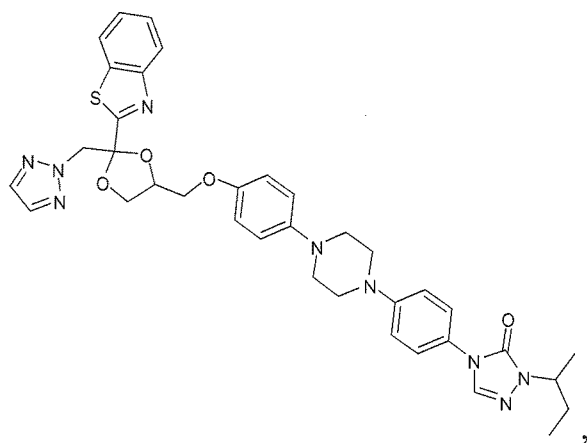


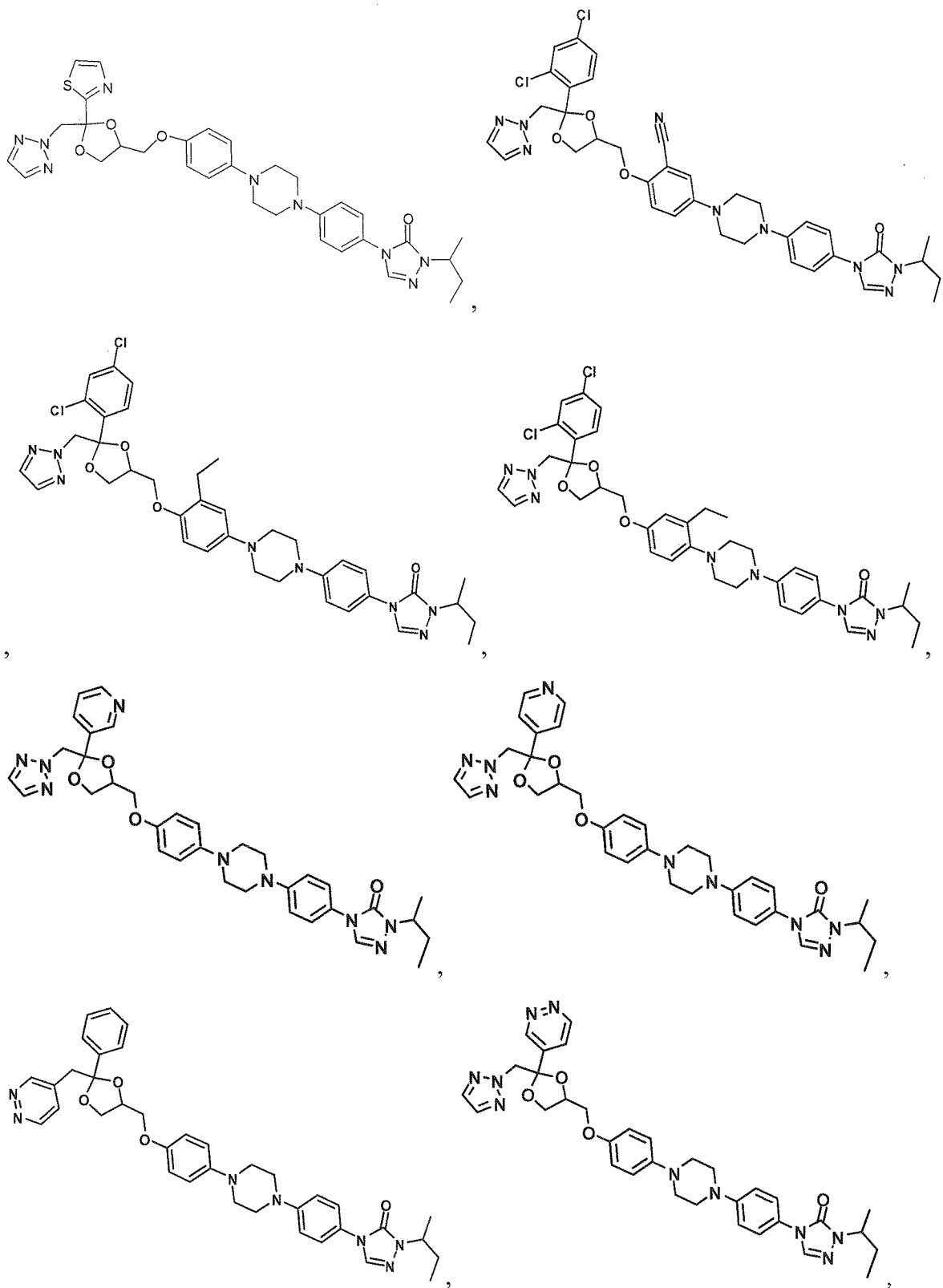


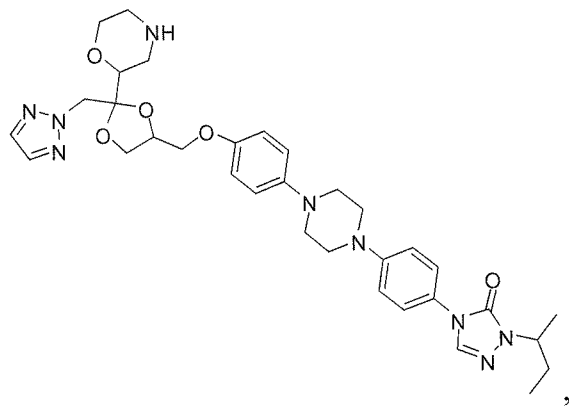
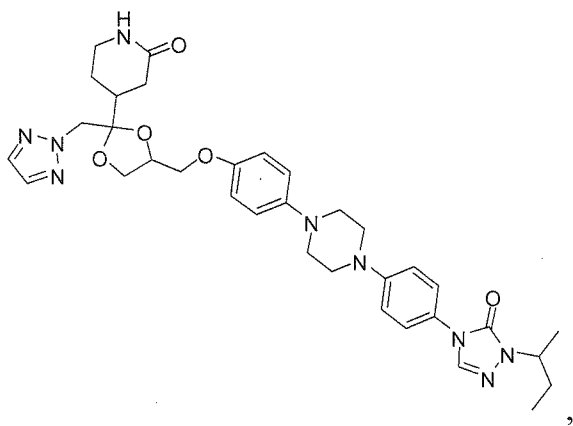
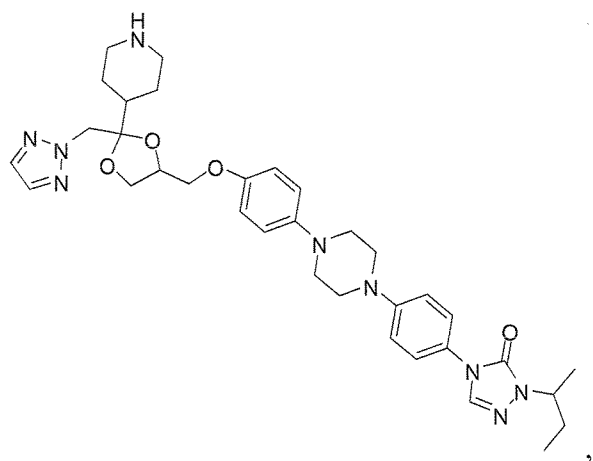
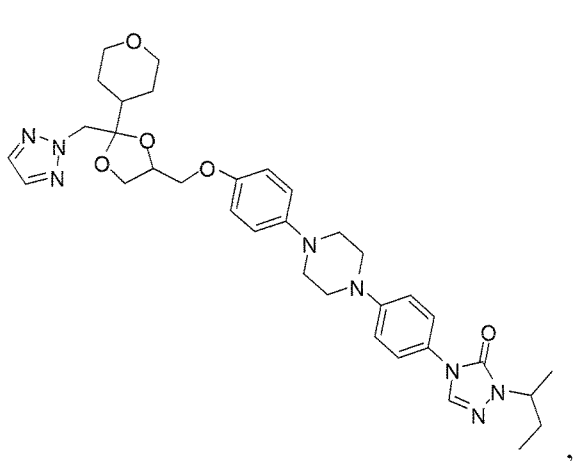
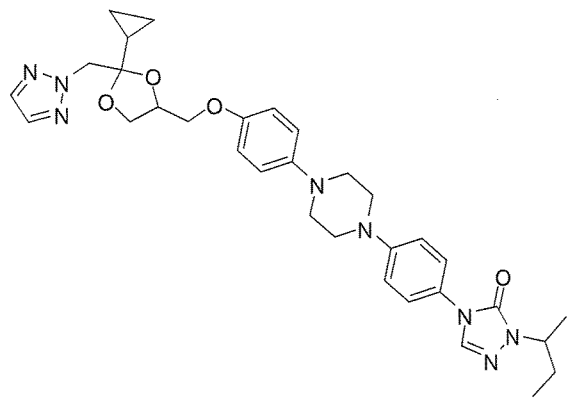
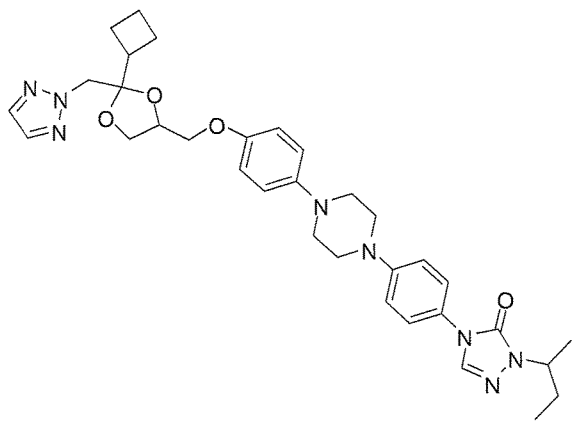
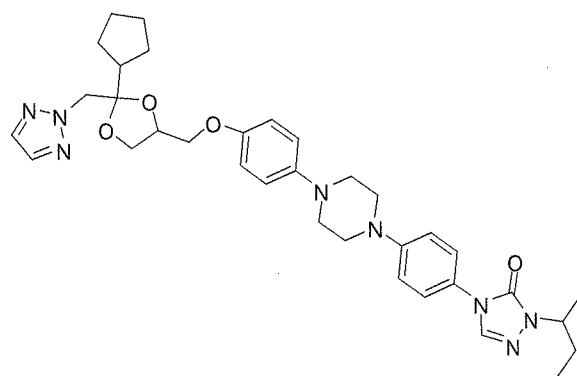
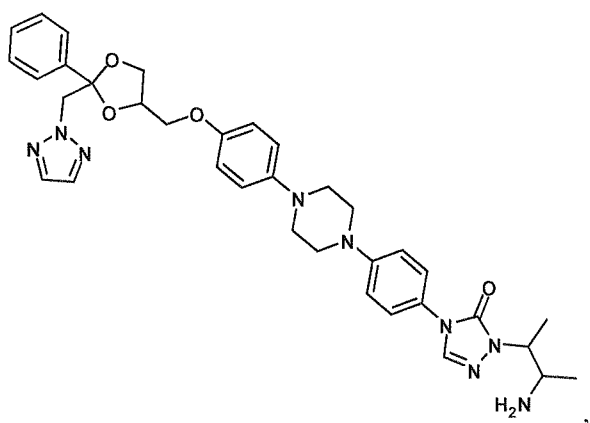


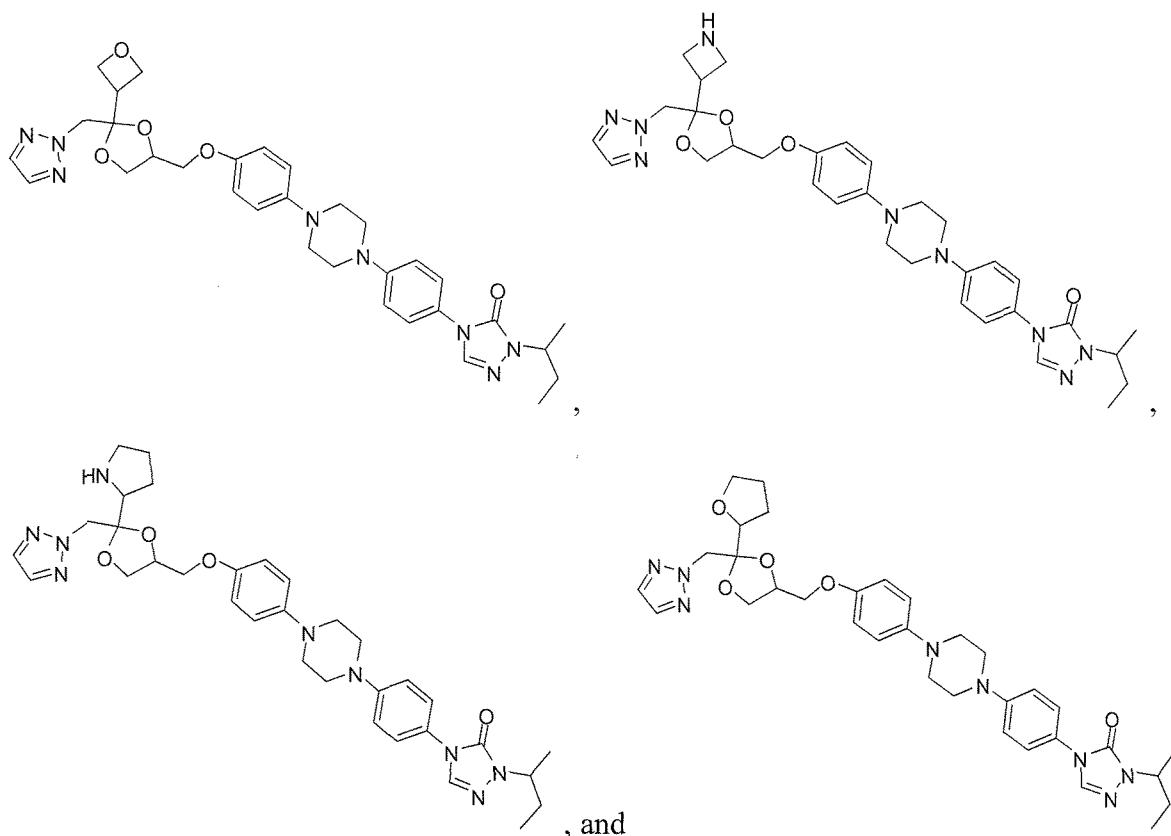




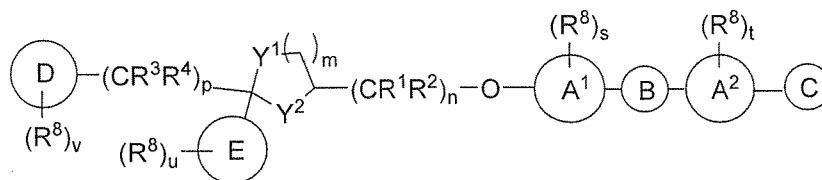








15. The use of any one of claims 1-14, wherein the fibrosis is liver fibrosis, idiopathic pulmonary fibrosis, kidney fibrosis, or cardiac fibrosis.
16. The use of claim 15, wherein the liver fibrosis is associated with the later stages of alcoholic or nonalcoholic liver cirrhosis.
17. The use of claim 15, wherein the fibrosis is idiopathic pulmonary fibrosis.
18. The use of any one of claims 1-14, wherein the disease or disorder characterized by fibrosis is a chronic autoimmune disease.
19. The use of claim 18, wherein the chronic autoimmune disease is rheumatoid arthritis, scleroderma, Crohn's disease or systemic lupus erythematosus.
20. The use of claim 19, wherein the chronic autoimmune disease is scleroderma.
21. The use of any one of claims 1-14, wherein the fibrosis is keloid formation resulting from abnormal wound healing.
22. The use of any one of claims 1-14, wherein the fibrosis occurs after organ transplantation.
23. A compound of Formula (II), a pharmaceutically acceptable salt, solvate, stereoisomer, or isomer thereof:



Formula (II)

wherein:

A^1 and A^2 are independently selected from aryl or heteroaryl;

B is ;

C is or ;

D is or ;

E is aryl, heteroaryl, carbocyclyl, heterocyclyl, or alkyl;

each R^1 , R^2 , R^3 , and R^4 is H;

R^7 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, alkylene($NR^{13}R^{14}$), cycloalkyl, heterocyclyl, -alkylene(cycloalkyl), or -alkylene(heterocyclyl);

each R^8 is independently selected from alkyl, cycloalkyl, heterocyclyl, halo, hydroxy, nitrile, azido, nitro, alkoxy, haloalkoxy, haloalkyl, hydroxyalkyl, alkoxyalkyl, -alkylene($NR^{13}R^{14}$), -alkylene(cycloalkyl), -alkylene(heterocyclyl), aryl, heteroaryl, $-SR^{13}$, $-SOR^{13}$, $-SO_2R^{13}$, $-SO_2NR^{13}R^{14}$, $-NR^{13}R^{14}$, $-NR^{13}SO_2R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$, $-NR^{13}C(O)NR^{13}R^{14}$, $-C(O)R^{14}$, $-C(O)OR^{14}$, and $-C(O)NR^{13}R^{14}$; or two adjacent R^8 form a heterocyclyl ring;

each R^{13} and R^{14} is independently selected from H, alkyl, cycloalkyl, heterocyclylalkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, arylalkyl, heteroarylalkyl, aryl, and heteroaryl; or R^{13} and R^{14} taken together form a heterocycle with the atoms to which they are attached;

Y^1 and Y^2 are O;

n is 1, 2, or 3;

m is 1 or 2;

p is 1, 2, 3, or 4;

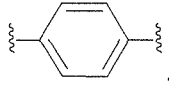
s is 0, 1, 2, 3, or 4;

t is 0, 1, 2, 3, or 4;

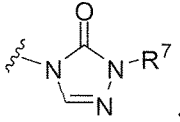
u is 0, 1, 2, 3, 4 or 5; and

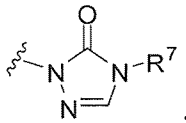
v is 0, 1, 2, 3, or 4.

24. The compound of claim 23 wherein A¹ is .

25. The compound of claim 23 or 24, wherein A² is .

26. The compound of claim 23 or 24, wherein A² is pyridine, pyrazine, pyrimidine, pyridazine, or triazine.

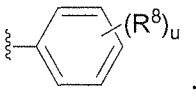
27. The compound of any one of claims 23-26, wherein C is .

28. The compound of any one of claims 24-26, wherein C is .

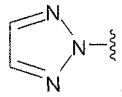
29. The compound of any one of claims 23-28, wherein E is cycloalkyl.

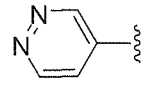
30. The compound of claim 29, wherein E is cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

31. The compound of any one of claims 23-28, wherein E is heterocyclyl.

32. The compound of any one of claims 23-28, wherein E is .

33. The compound of any one of claims 23-28, wherein E is heteroaryl.

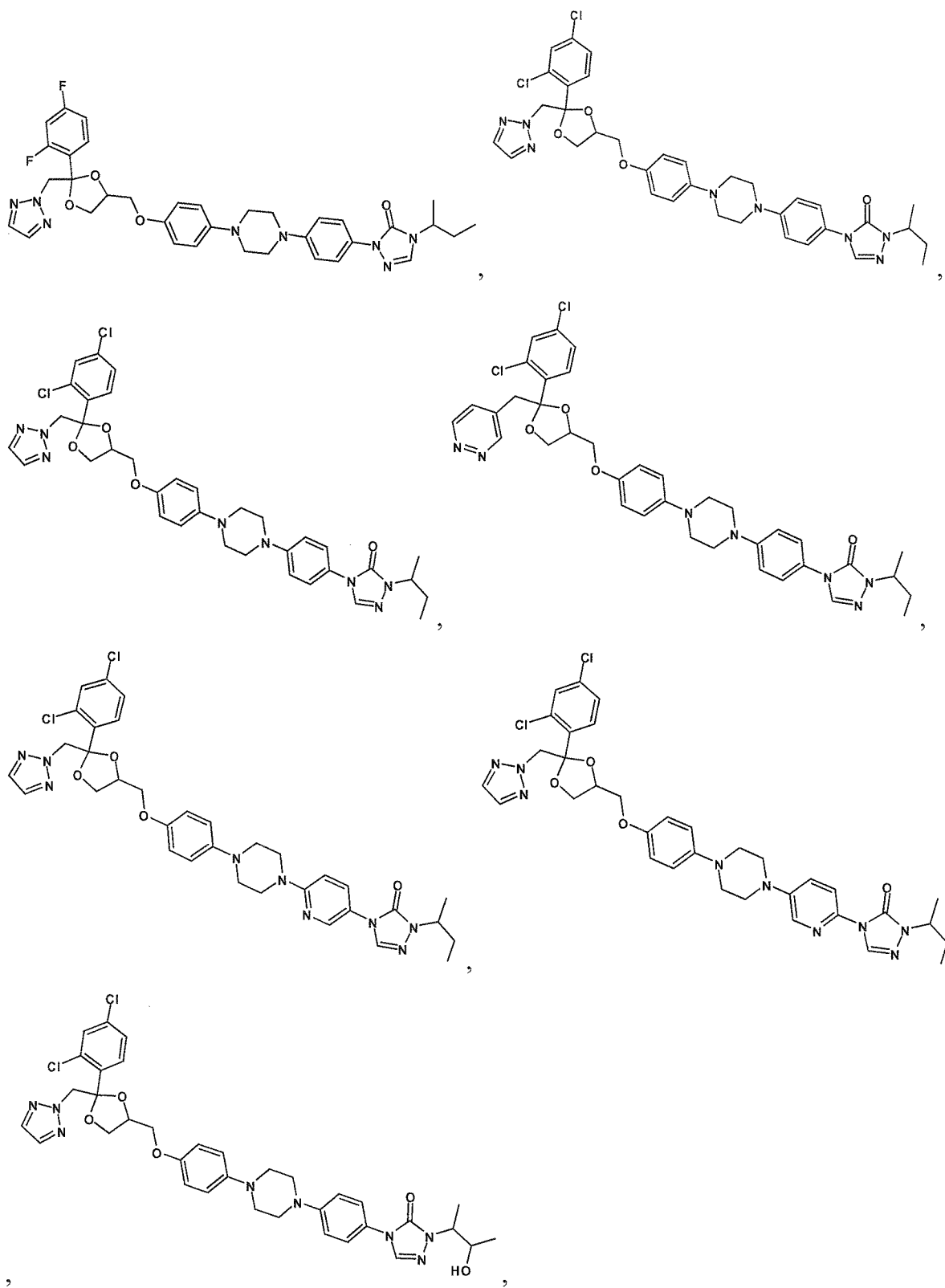
34. The compound of any one of claims 23-33, wherein D is .

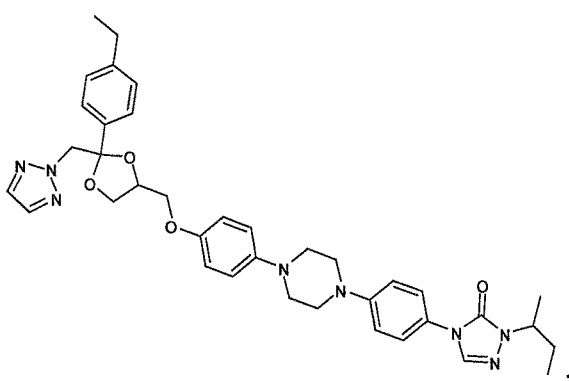
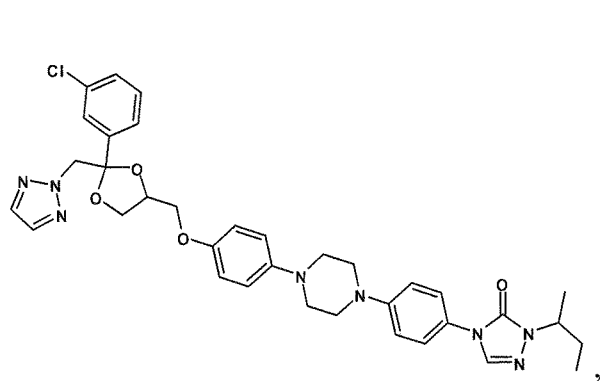
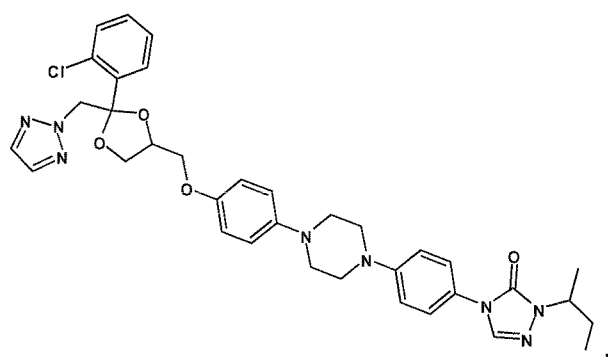
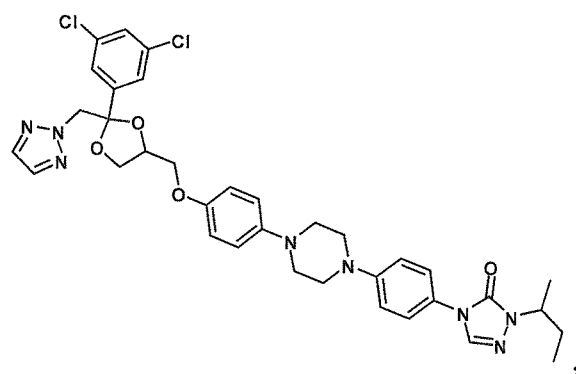
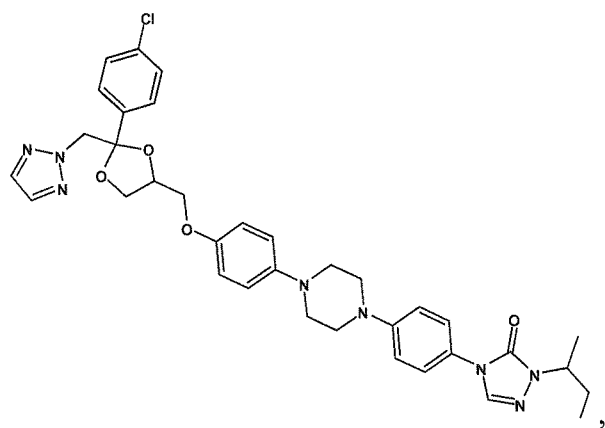
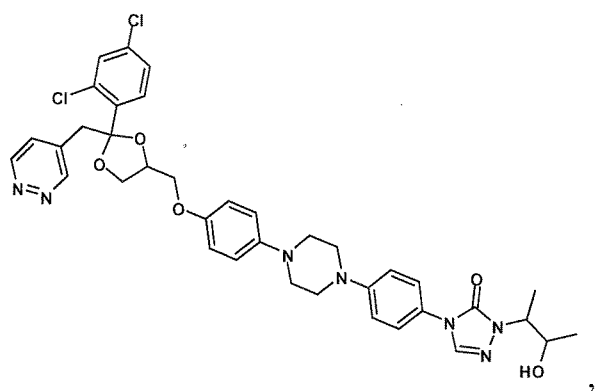
35. The compound of any one of claims 23-33, wherein D is .

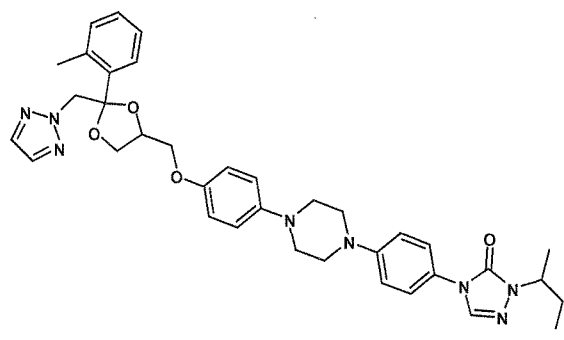
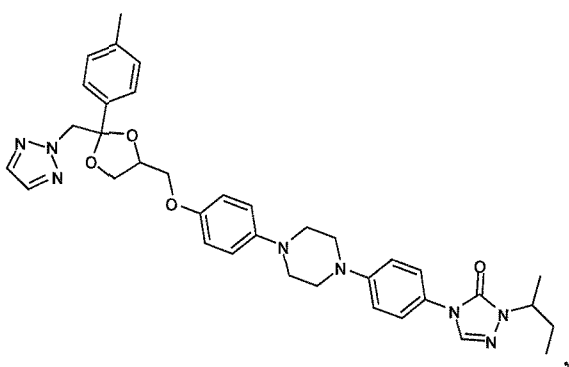
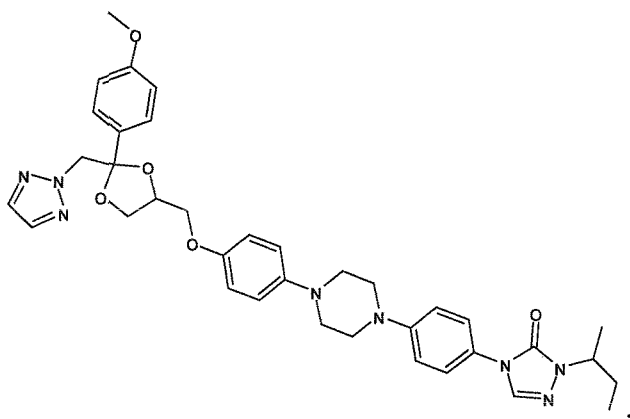
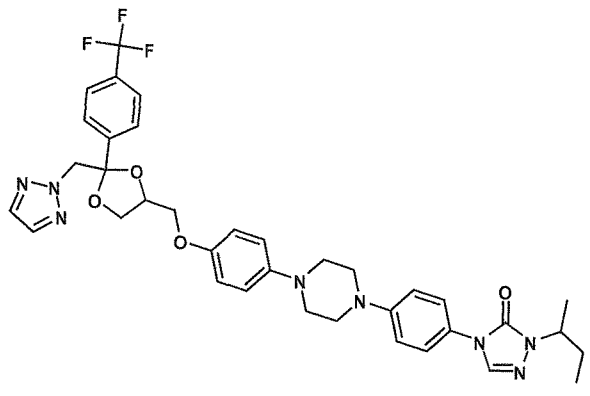
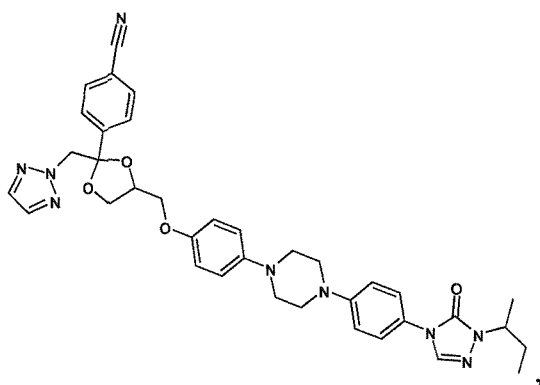
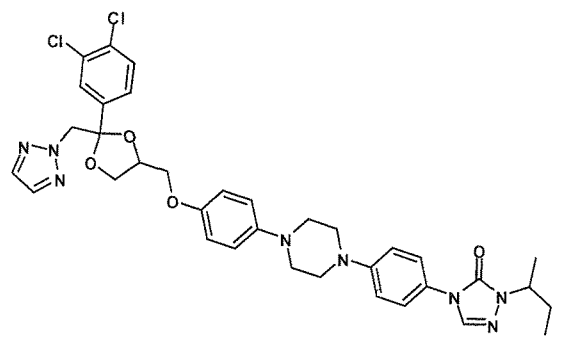
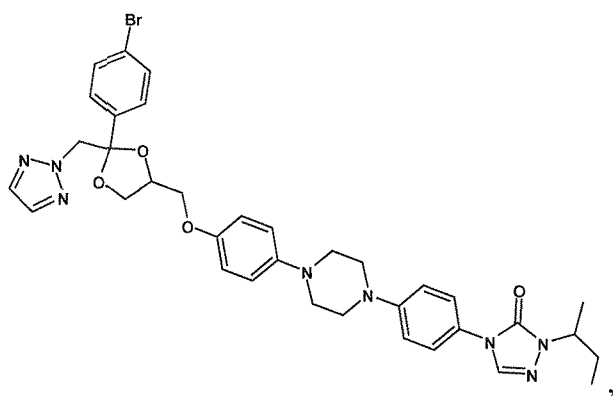
36. The compound of any one of claims 23-35, wherein p is 1, 2, or 3.

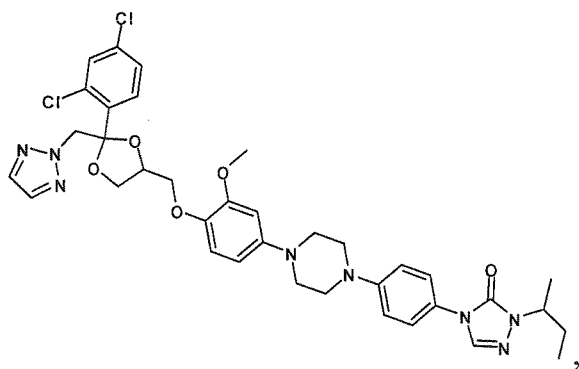
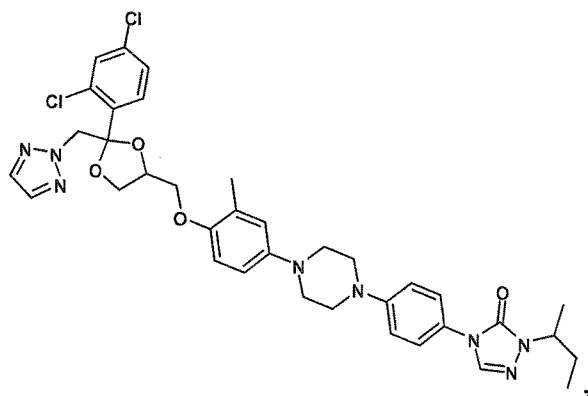
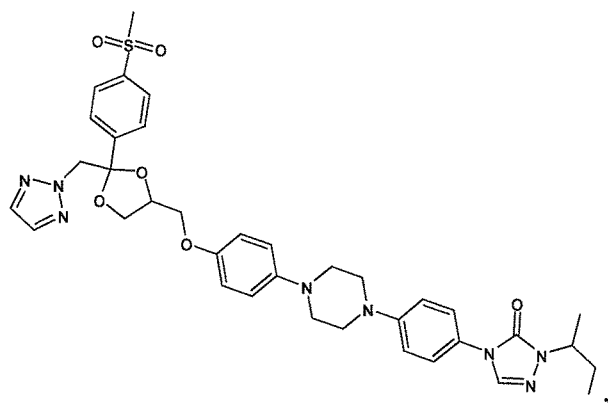
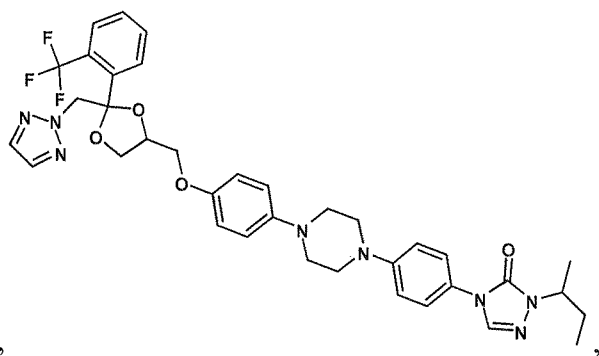
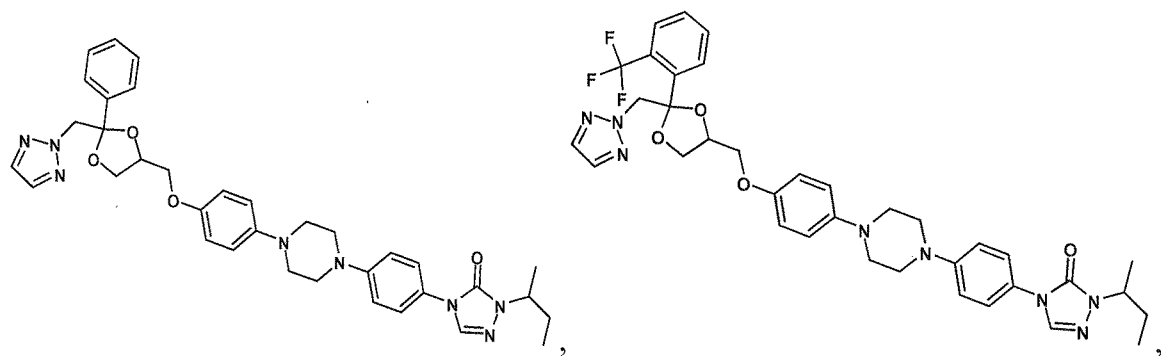
37. The compound of claim 36, wherein p is 1.

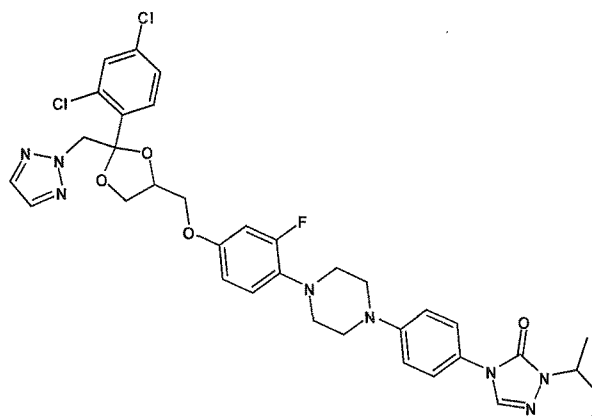
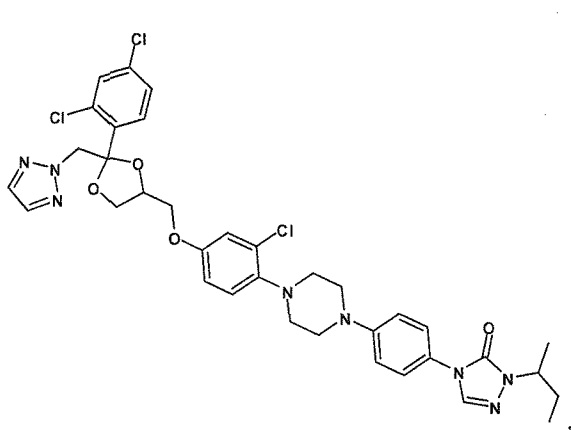
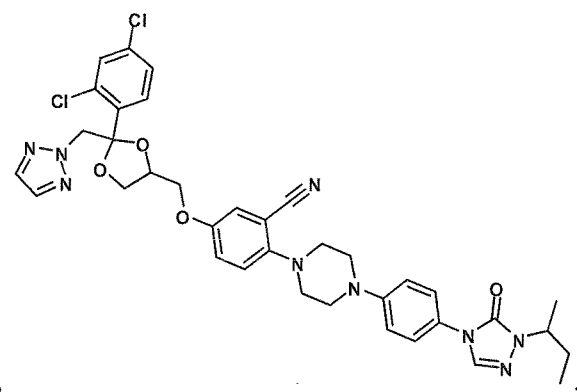
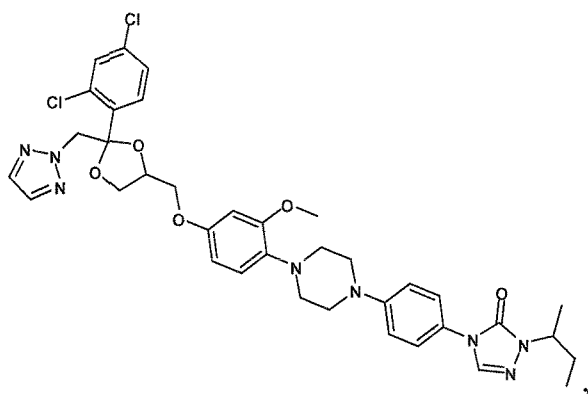
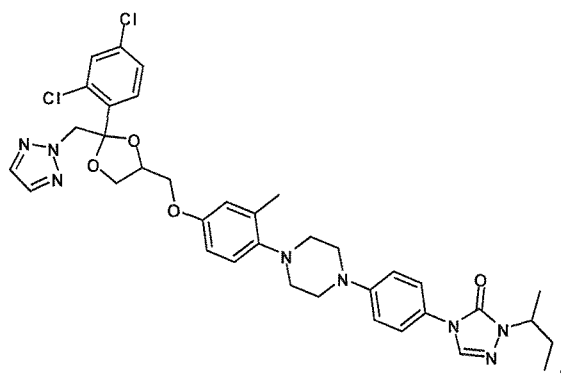
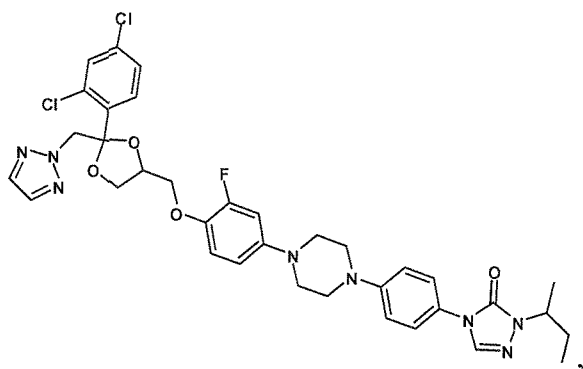
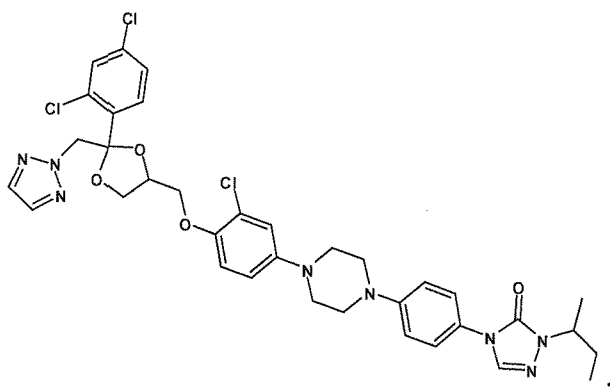
38. The compound of claim 23, wherein the compound is selected from:

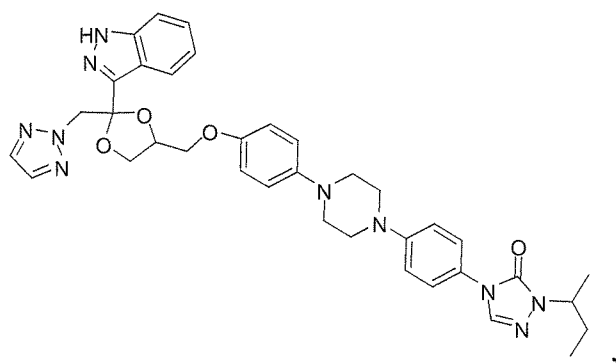
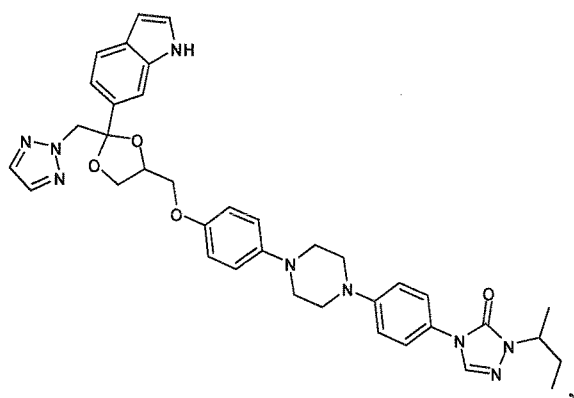
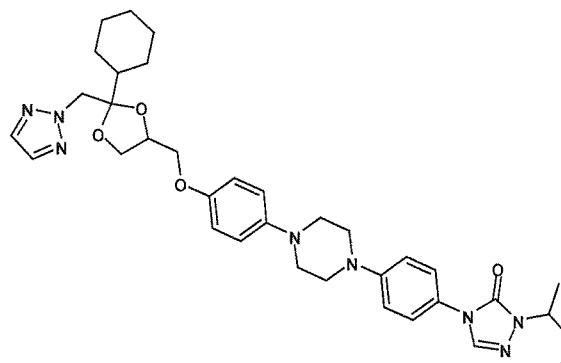
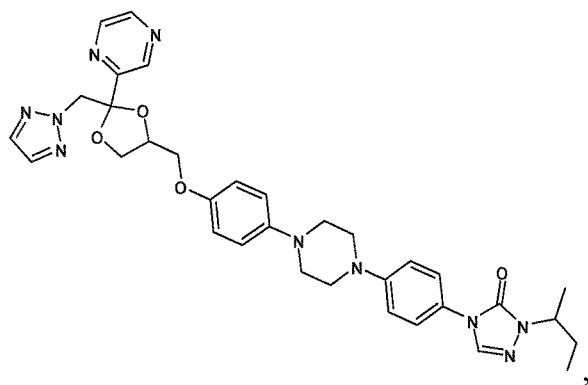
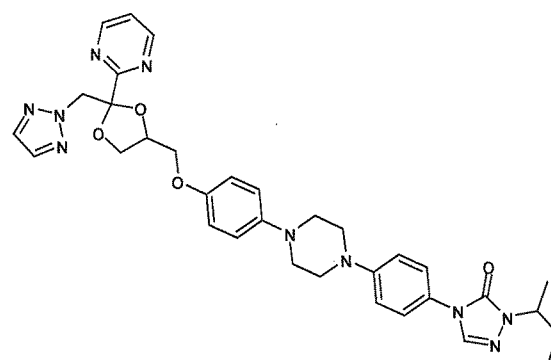
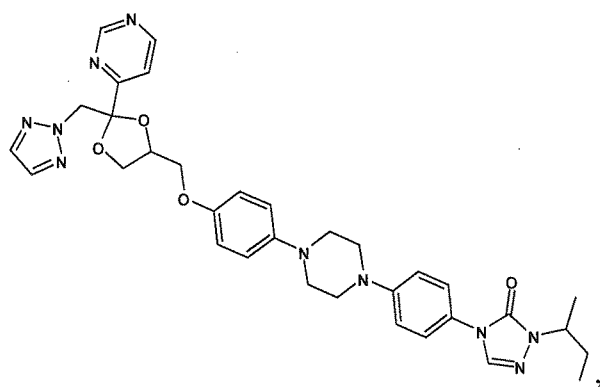


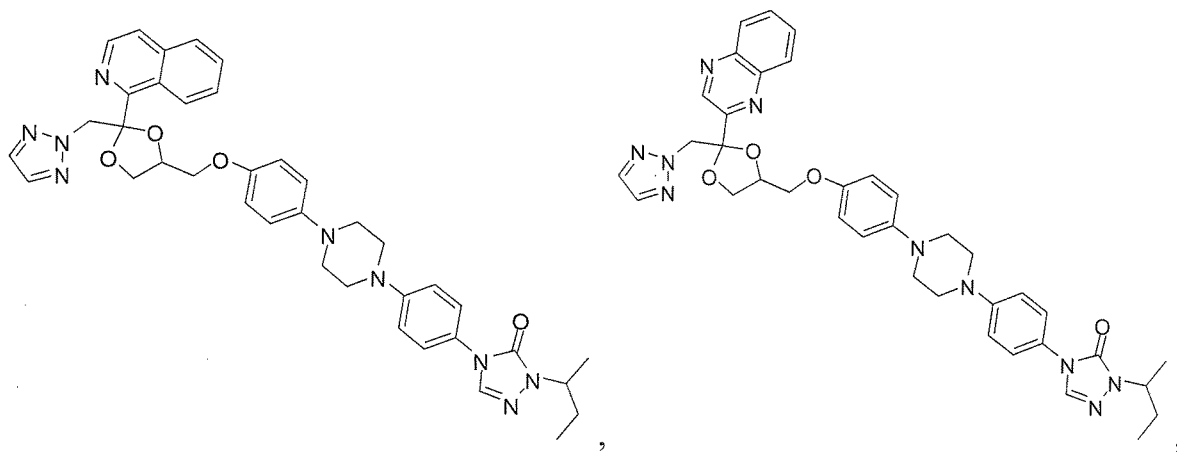
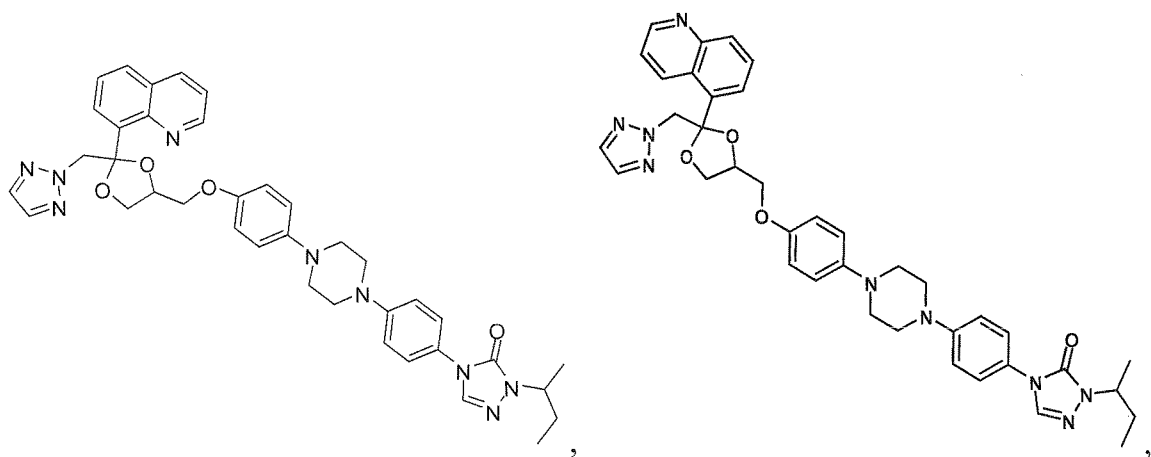
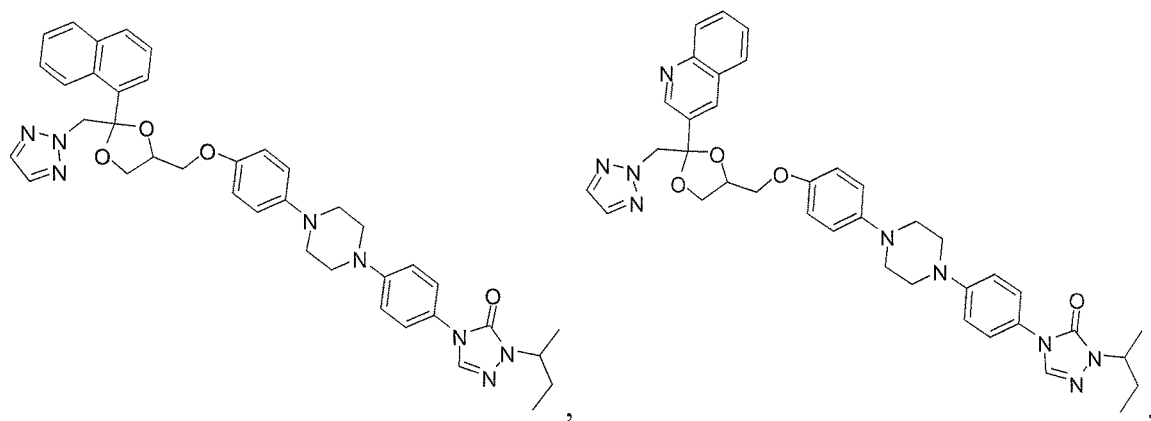
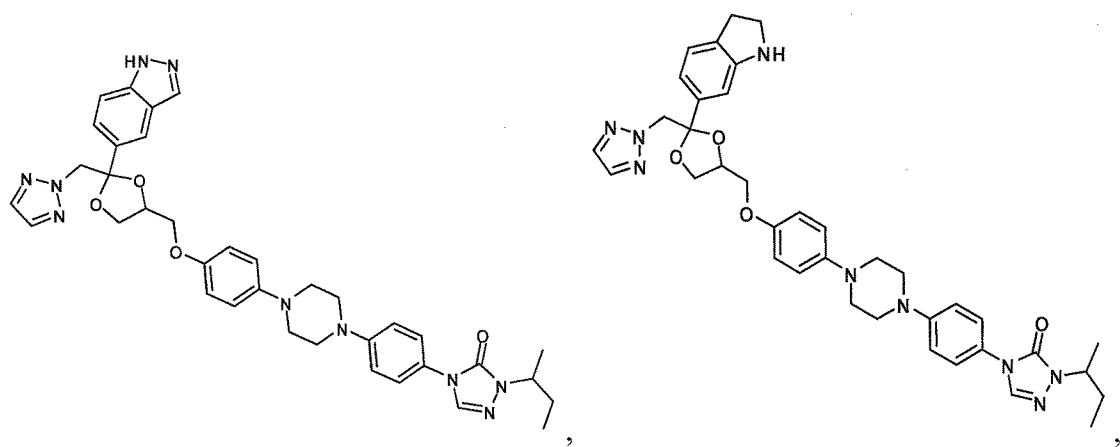


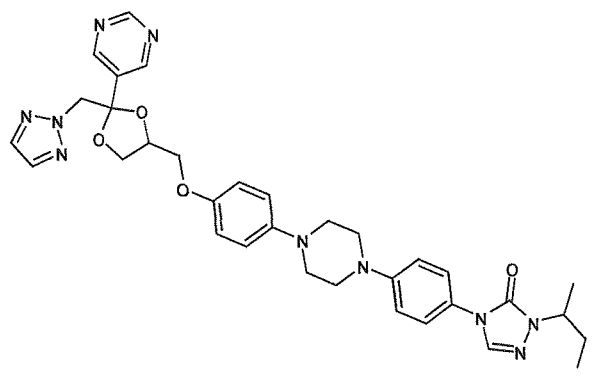
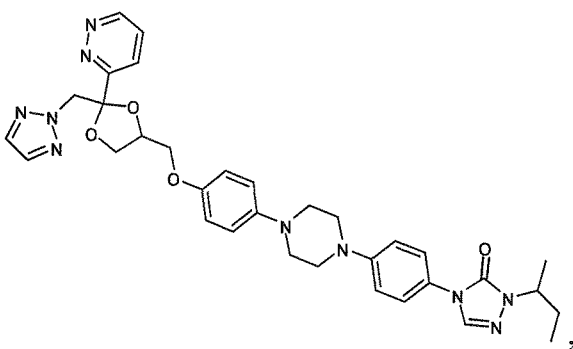
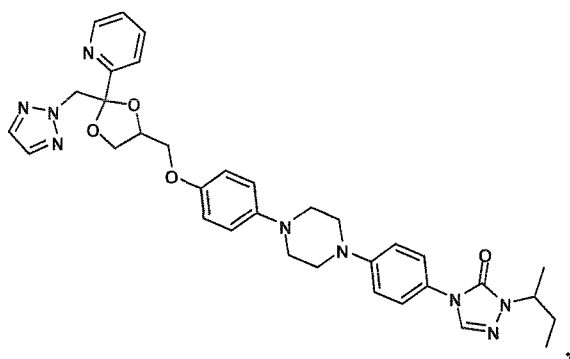
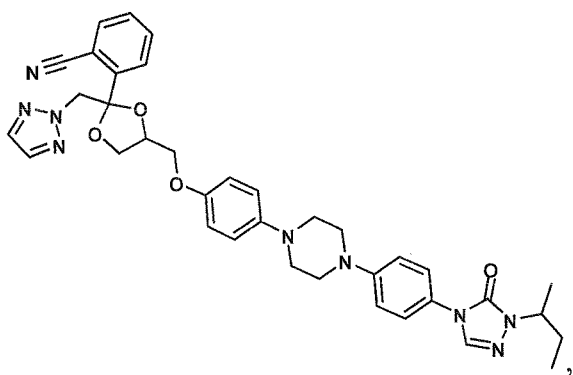
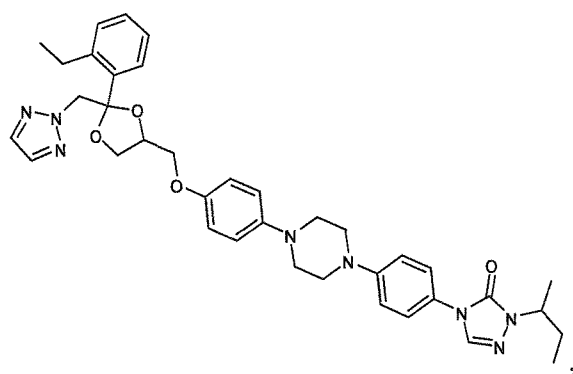
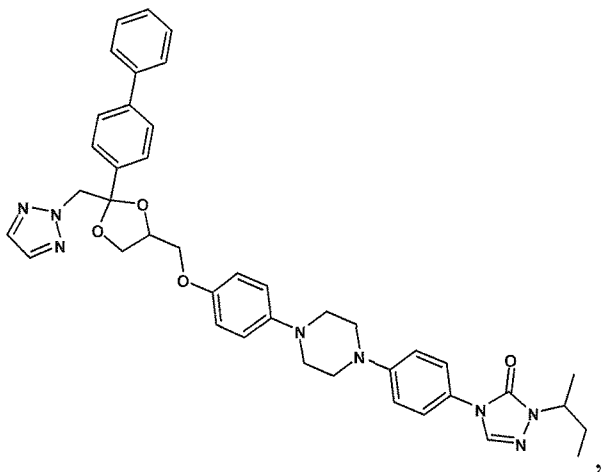
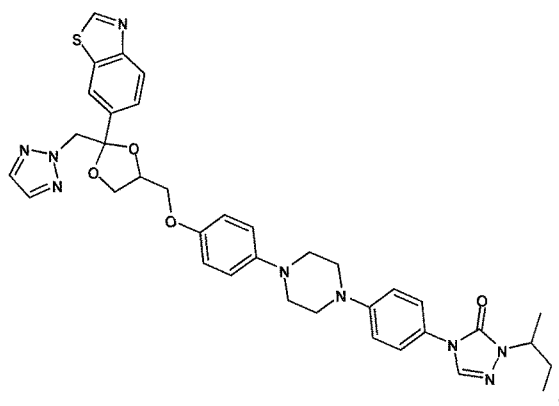
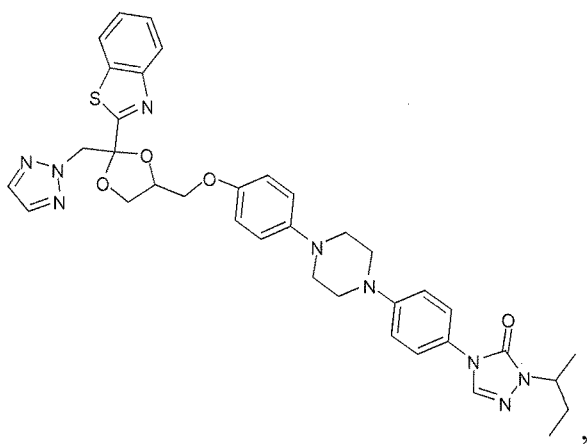


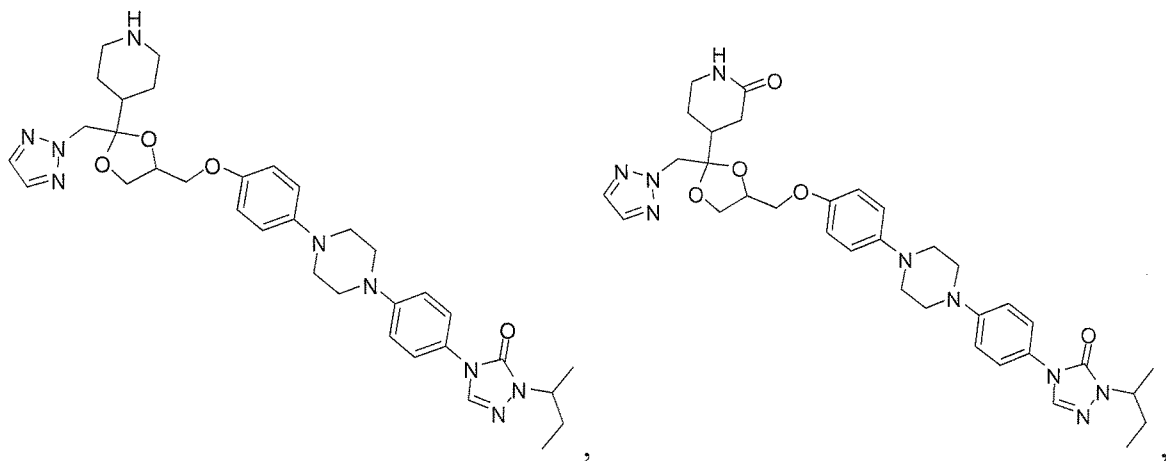
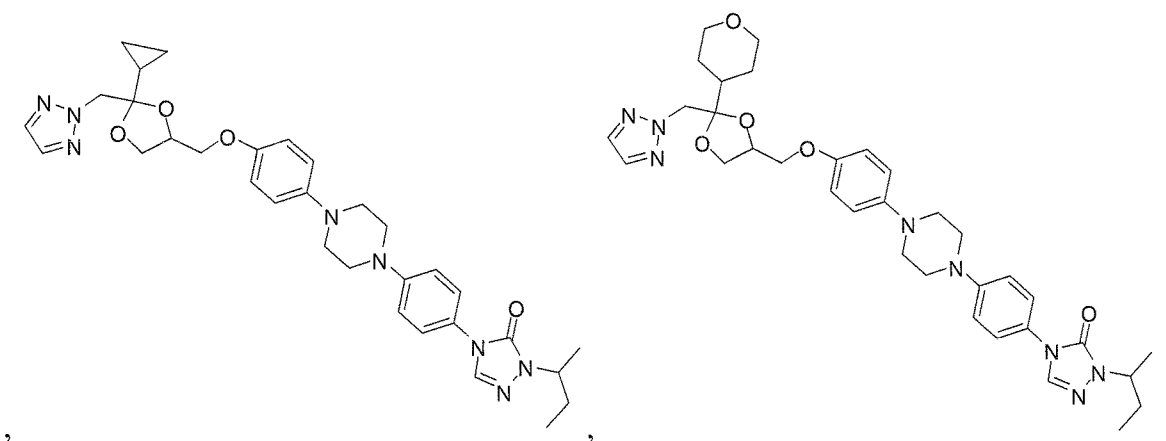
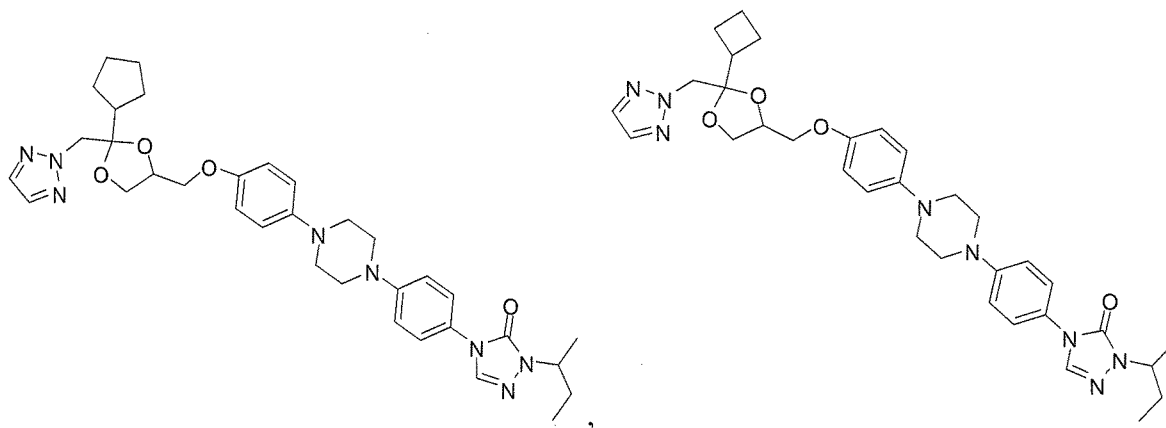
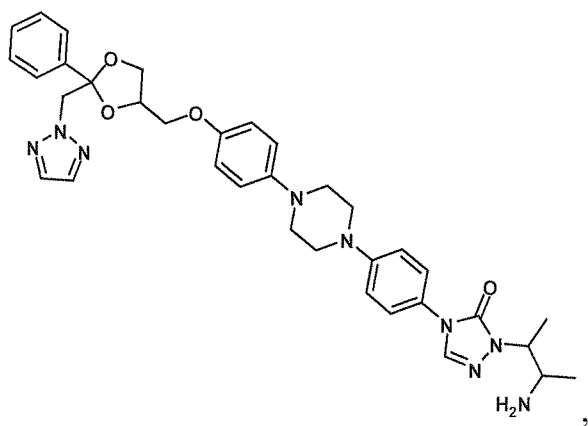


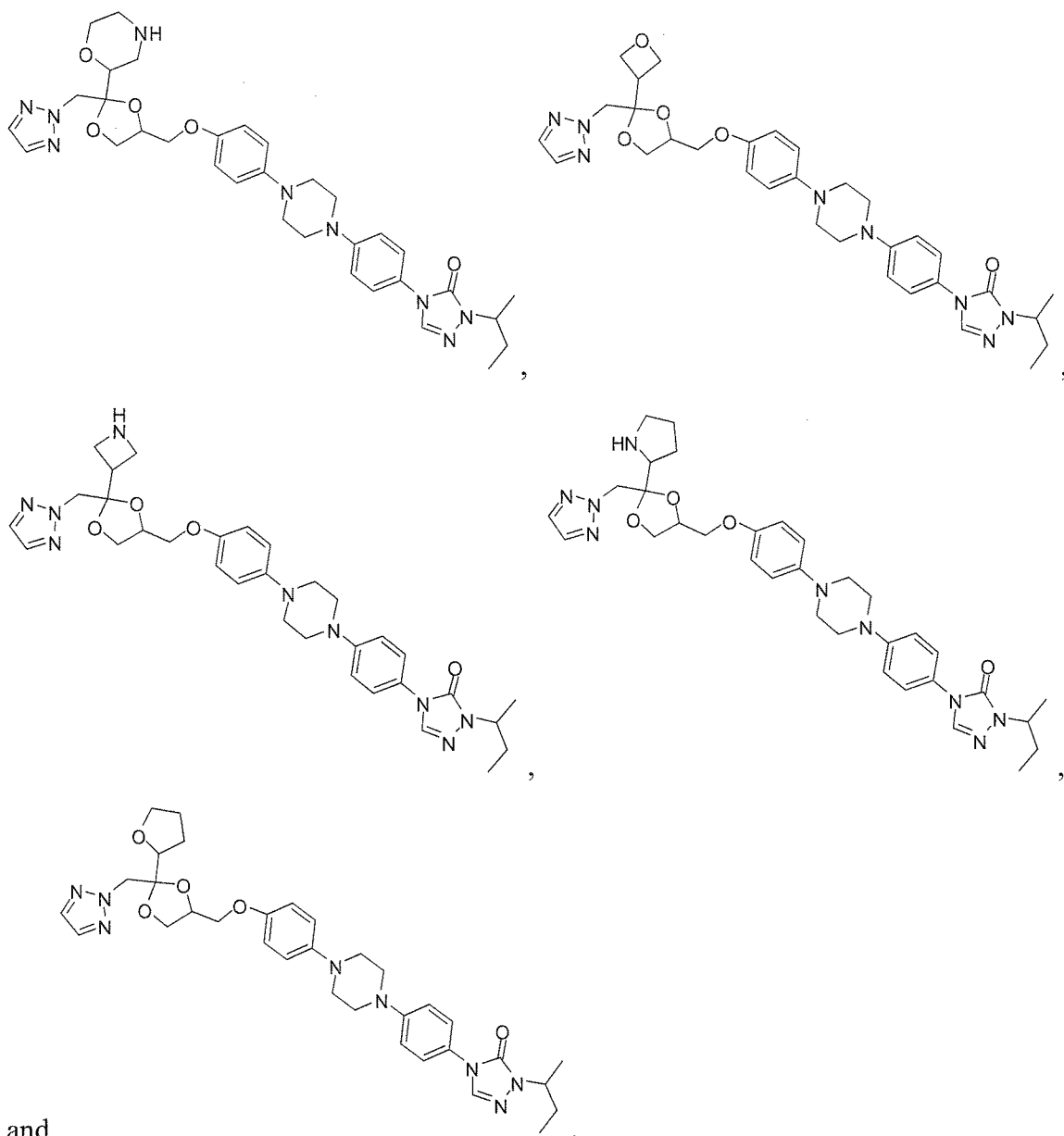












39. A pharmaceutical composition comprising a compound of any one of claims 23-38, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isomer thereof, and a pharmaceutically acceptable excipient.