

2018 07 06 .

2019 3 21 .

2020 06 22 .

2020 08 17 .

Prezcobix

Darunavir and Cobicistat Tablets

Dalunawei Kaobisita Pian

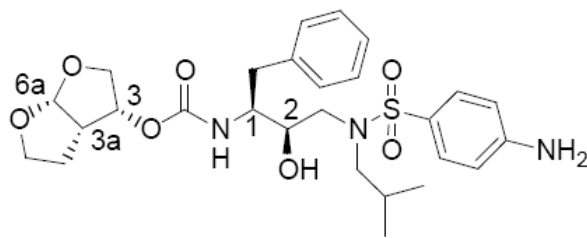
800 mg

867.28 mg

150 mg

[1S 2R -3-[[4-

]- 3R 3aS 6aR - [2 3-b]. -3-



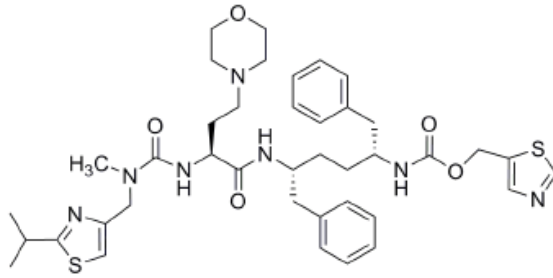
$C_{27}H_{37}N_3O_7S$

547.66

1,3- -5- [2R,5R -5-[[2S -2-[{[2- -2- -1,3-

-4-] }]-4- -4-] }-1,6- -2-

]



C₄₀H₅₃N₇O₅S₂

776.0

HIV

V11I V32I L33F I47V I50V I54M I54L

T74P L76V I84V L89V

800mg

867.28mg

150mg

HIV

HIV

HIV

12

12

<70 ml/min

Child-Pugh A

Child-Pugh B

Child-Pugh C

HIV

III

GS-US-216-130 N=313

66.5%

1

58.4

28%

23%

16%

2

0.6%			1	0.3%
	/	N=2613		
/		600/100 mg	51.3%	1
		95.3		
96	/	800/100 mg	1	
	/	600/100 mg	2	
	/	800/100 mg	1	162.5
		192		
		SOC		1
		<1/10		

	Stevens-Johnson *
	*
	*

* / /

/ /

4 800mg

1 150mg 1

2.2%

HIV NRTI CPK

HIV

CART

	HIV			CART	
				Graves'	
				0.4mg/dl	
		1/	N=12		eGFR
50-79 ml/	N=18	I			
		150 mg	7		eGFR _{CG}
Cockcroft-Gault					-9.9 ±
13.1mL/				-11.9 ± 7.0mL/	
	eGFR _{CG}				
III	GS-US-216-130		2	eGFR _{CG}	
48	eGFR _{CG}		2	-9.6 ml/min,	48 -9.6 ml/min
					1968
					236
HBV	HCV				
1.					
2.	Child-Pugh C				
3.		P450 3A	CYP3A		
		CYP3A			
-		1-			
-					

-

- /

-

-

-

- /

- / DAA

- /

- PDE-5

-

-

-

4. CYP3A

-

-

-

\ ñ > /Span <<MCID 53 4BDC /C2_0 HIVTd [<4221122C0872>10.9 <75F0A26>10.8

..... / +

5.

6.

..... /

N=3,063

0.5%

AST/ALT

..... /

7.

70 ml/min

HIV

A B

HIV

HIV

HIV

8.

HIV /

CART

BMI

9.

HIV

PK

11.

12.

7. 2 3. 3 1. 6-12

6. 5.

/.

HIV

3-17

3-17

3.

65

CYP3A CYP2D6 P
 CYP3A CYP2D6 P
 MATE1 OATP1B1 OATP1B3 CYP1A2
 CYP2B6 CYP2C8 CYP2C9 CYP2C19 CYP1A2
 CYP3A4 CYP2C9 CYP2C19 UGT1A1 P-gp (MDR1)
 CYP3A / CYP2D6
 /
 CYP3A
 2
 CYP3A CYP3A
 CYP3A

2

HIV-1	NRTIs	
	↔ ↔ ↔	1 2
	↔ ↔ ↑	P
NRTIs	↔	NRTIs

HIV-1	NNRTIs.
	↑ ↑ ↑	/ CYP3A
	↓ ↓ ↓ ↑	/ NNRTI CYP3A NNRTI
	↔ ↔ ↑	CYP3A
HIV-1 .	CCR5	
	↑	CYP3A 150mg
HIV-1 .	.	
	↔ ↔	
	↑	CYP3A
	↔ ↔	
. . . . / . .	↑ / .	CYP3A / CYP2D6

	↑	P
	↔ ↑ ↑	CYP3A
	↑	CYP3A
DOACs	↑DOACs	DOACs CYP3A4 / P-gp DOAC P-gp CYP3A4 DOAC DOAC CYP3A4 P-gp /
		CYP3A /

	↑	CYP3A CYP3A
	↑	CYP2D6 / CYP3A
	↑	
	↑ ↑ ↑ ↑	CYP3A / P / 200 mg/
	↑	
	↑	CYP3A
/	↔ ↑ ↑	/ CYP3A /
	↓ ↓ ↑	CYP3A / 150 mg

	↓ ↔	
	↑	CYP2D6
	↑	CYP3A
	↑ ↓ ↓	
CYP3A	↓ ↓ ↑	CYP3A
	↓ ↓ ↑ ↑	
	↑	
	↓ ↓	CYP3A
	↑	
H ₂	↔ ↔	H ₂

		H ₂
HCV. glecaprevir/ pibrentasvir	↑ ↑glecaprevir ↑pibrentasvir ↓ ↓	OATPB1 CYP3A /glecaprevir /pibrentasvir glecaprevir pibrentasvir P-gp BCRP / OATP1B1/3. glecaprevir /pibrentasvir
	↓	CYP3A
HMG-CoA	↑HMG-CoA	HMG-CoA CYP3A / HMG-CoA 10 mg/
	↑	
	↑	CYP3A
	↑	CYP3A QT
	↑	CYP2D6 / CYP3A
/	↔ ↑ ↔ ↓	

	↑	CYP3A CYP2D6 CYP3A
	↑	
PDE-5 . .	↑PDE-5 .	PDE-5 . PDE-5 . CYP3A PDE-5 . • • 20mg 40mg 24 1 20mg 40mg PDE-5 . 48 25mg 72 2.5mg 72 10mg PDE-5 .
	↑	CYP3A / P
	↔ ↔	

/	↑ /	/ CYP3A /
	↑	
	↑	
↔	↑	↓

3200mg

1600mg

60

400 mg

150

mg

800 mg

100 mg

800 mg

150 mg

GS-US-216-0130 24

ARTEMIS

ODIN

/

800/100 mg

800/150 mg

GS-US-216-0130 313 HIV-1 295 18

800 mg 150 mg

HIV-1

HIV-1 RNA 1000 /mL HIV-1 RNA

<50 /mL

313 35 18~72 89.1% 59.7%

34.5% 21.7% 1.3%

HIV-1 RNA CD4+ 4.8 log₁₀ /mL 370×10⁶

/L 6~1473×10⁶ /L 4.8 log₁₀ /mL 107×10⁶ /L 5~643

×10⁶ /L 3

3 GS-US-216-0130 24

	800/150 mg. + OBR N=295	800/150 mg. + OBR N=18	800/150 mg. + OBR N=313
HIV-1 RNA < 50 /mL	83.7%	61.1%	82.4%
†	9.8%	38.9%	11.5%
24 ‡	4.7%	0	4.5%
§	1.0%	0	1.0%
¶	0.7%	0	0.6%
N =			
†	24	24	
‡	20~30		
§	1		
¶		< 50 /mL	

GS-US-216-0130 III TMC114FD2HTX3001 AMBER

/ +FTC/TDF
 48 88.4% HIV-1 RNA <50 /mL;
 / 800/100 mg
 / HIV-1
 TMC114-C211 192
 HIV-1
 TMC114-C214 96
 HIV-1 IIb TMC114-C213
 TMC114-C202 96
 TMC114-C211
 TMC114-C211 III
 HIV-1 / 800/100mg
 / 800/200mg
 300mg TDF
 200mg FTC
 HIV-1 HIV- /mL
 HIV-1 RNA <100,000 /mL /mL
 CD4+ <200 /mm³ /mm³
 HIV-1 RNA < 50 /mL
 TMC114-C211 192 689
 / /
 4 TMC114-C211 / 800/100mg
 / 800/200mg
4 TMC114-C211

	TMC114-C211	
	800/100mg + TDF/FTC N = 343	800/200mg + TDF/FTC N = 346
	34 18~70	33 19~68
	70%	70%
	30%	30%

	40%	45%
	23%	21%
	23%	22%
	13%	11%
log ₁₀ copies/mL	4.86	4.84
CD4+ /mm ³	228	218
	4~750	2~714
100,000 copies/mL	34%	35%
CD4+ <200 /mm ³	41%	43%

TMC114-C211 / 800/100mg 192

5

5 192 TMC114-C211

	800/100mg + TDF/FTC N = 343	800/200mg + TDF/FTC N = 346
HIV-1 RNA < 50 /mL	70%*	61%
†	12%	15%
‡	5%	13%
§	13%	12%
¶	<1%	0%

N =
 * 95%CI 1.9; 16.1
 † 192 192
 ‡ 186~198
 § 1
 ¶ < 50 /mL

TMC114-C211 192 / 800/100mg

CD4+ 258 /mm³ /
 800/200mg 263 /mm³ 48 <50 /mL
 / 192 81% / 68%
 192 ITT OP / /

TMC114-C229

TMC114-C229

V11I V32I L33F I47V I50V I54L I54M T74P
 L76V I84V L89V 1,000 HIV-1 RNA /mL
 HIV-1 / 800/100mg /
 600/100mg 2 2

NRTIs

HIV-1

HAART 12 HIV-1 RNA 50
 /mL 48 590
 6 TMC114-C229 / 800/100mg
 / 600/100mg

6 TMC114-C229

	TMC114-C229	
	800/100mg+ OBR N = 294	600/100mg + OBR N = 296
	40 (18~70)	40 (18~77)
	61%	67%
	39%	33%
	35%	37%
	28%	24%
	16%	20%
	16%	14%
log ₁₀ copies/mL	4.19	4.13
CD4 /mm ³	219 (24~1306)	236 (44~864)
100,000 copies/mL	13%	11%
CD4 <200 /mm ³	43%	39%
	0.50 (0.1~1.8)	0.50 (0.1~1.9)
PI	3	4
NNRTI	2	1
NRTI	1	1
PIs	88%	86%

0	84%	84%
1	8%	9%
2	5%	4%
	3%	2%
ARVs		
NRTIs	3	3
NNRTIs	1	1
PIs	1	1
* Antivirogram®		
†Johnson VA, Brun-Vézinet F, Clotet B, et al. Update of the drug resistance mutations in HIV-1: December 2008. Top HIV Med 2008; 16(5): 138-145		
‡ ARVs		
OBR		

TMC114-C229 / 800/100mg 48

7

7 48 TMC114-C229

	TMC114-C229	
	800/100mg + OBR N = 294	600/100mg + OBR N = 296
HIV-1 RNA < 50 /mL	69%	69%
*	26%	23%
48		
†		
‡	3%	4%
§	2%	3%
¶	0%	<1%

N =

* 48 48

AE

AEs/

/mL

† 42-54

‡ 1

§

< 50 /mL

/ 600/100mg / 400/100mg
 OBR 2 NRTIs
 NNRTIs
 HIV-1 HIV-1 RNA > 1000 /mL
 12 HAART
 HIV-1 RNA < 400 /mL TMC114-C214
 96 595
 / /
 8 TMC114-C214 / 600/100mg
 / 400/100mg

8 TMC114-C214

	TMC114-C214	
	600/100mg+ OBR N = 298	400/100mg + OBR N = 297
	40 (18~68)	41 (22~76)
	77%	81%
	23%	19%
	54%	57%
	18%	17%
	15%	15%
	9%	9%
log ₁₀ copies/mL	4.33	4.28
CD4 /mm ³	235 (3~831)	230 (2~1096)
100,000 copies/mL	19%	17%
CD4 <200 /mm ³	40%	40%
	0.60 (0.10~37.40)	0.60 (0.1~43.8)
	0.70 (0.40~74.40)	0.80 (0.30~74.50)
	*	
PI	4	4
NNRTI	1	1
NRTI	2	2

*		
2	78% 8% 13%	80% 9% 11%
ARVs †		
NRTIs	4	4
NNRTIs	1	1
PIs	1	1
‡ §PI		
‡	2%	3%
*Johnson VA Brun-Vezinet F Clotet B et al. Update of the drug resistance mutations in HIV-1 Fall 2006. Top HIV Med 2006. 14. 3. 125-130		
† ARVs		
‡ Antivirogram®		
§ PIs		

TMC114-C214 / 600/100mg 96
9

9 96 TMC114-C214

	/. 600/100mg + OBR N = 298	/. 400/100mg + OBR N = 297
HIV-1 RNA < 50 /mL	58%	52%
*	26%	33%
96 †		
‡	7%	8%
§	8%	7%
‡	1%	<1%
N =		
* 96	96	
† 90-102		
‡ 1		
§ < 50 /mL		

TMC114-C214 96 / 600/100mg

CD4+ 81 /mm³ /

400/100mg 93 /mm³

TMC114-C213 TMC114-C202

TMC114-C213 TMC114-C202 PI

I Ib 2

/

600/100mg

HIV-1 HIV-1 RNA > 1000 /mL

PI s NNRTI s NRTI s 1 PI

D30N M46I/L G48V I50L/V V82A/F/S/T I84V L90M

8 PI PI

/ OBR

PI s OBR

ARV PI s OBR OBR 2 NRTIs

PI s 36% fos

34% 35% 17% 98%

PI 23% PIs

47% 35% ENF HIV-1 RNA

1 log₁₀

TMC114-C213 TMC114-C202 /

PI 10 TMC114-

C213 TMC114-C202 / 600/100mg

PI

10 TMC114-

	4.3	3.3
PI NNRTI NRTI	12 1 5	12 1 5
2	8% 22% 70%	9% 21% 70%
ARVs NRTIs NNRTIs PIs	6 1 5	6 1 5
‡PIs	63%	61%
†	20%	17%
*Johnson VA Brun-Vezinet F Clotet B et al. Update of the drug resistance mutations in HIV-1 Fall 2006. Top HIV Med 2006. 14 3. 125-130		
† Antivirogram®		
‡ PIs		

TMC114-C213 TMC114-C202 /
600/100mg 96 11
11 TMC114-C213 TMC114-C202 96

	TMC114-C213 TMC114-C202	
	600/100mg + OBR N=131	PI(s) + OBR N=124
96 1 log ₁₀ HIV-1 RNA 96 < 50 /mL	57% (39%)	10% (9%)
	29%	80%
*	8%	53%
†	17%	19%
‡	4%	8%
	9%	3%
	5%	7%
* 12 † 96 ‡ 96	0.5 log ₁₀ HIV-1 RNA 1 log ₁₀ 96 1 log ₁₀	1 log ₁₀

TMC114-C213 TMC114-C202 48 /
600/100mg PI HIV-1 RNA <400 /mL
55.0% 14.5% HIV-1RNA
/ 600/100mg 1.69 log₁₀ /mL PI 0.37 log₁₀
/mL CD4+ / 600/100mg
103 / mm³ PI 17 /mm³

HIV-1 CYP3A

Gag-Pol HIV-1 HIV-1

CYP3A P450 CYP3A

T /

HIV-1 HIV-2 EC₅₀ 1.2~

8.5 nM (0.7 ~ 5.0 ng/mL) HIV-1 M A B C D E F

G O EC₅₀ <0.1~4.3 nM

EC₅₀ 5.4

HIV /

HIV-1 HIV-1

HIV-1

HIV-1 HIV-1 21~88

2~4 S37D R41E/T K55Q H69Q K70E T74S

V77I I85V

9 HIV-1

22 L10F V11I I13V I15V G16E L23I V32I L33F

S37N M46I I47V I50V F53L L63P A71V G73S L76V V82I I84V T91A/S

and Q92R L10F V32I L33F S37N M46I I47V I50V L63P A71V I84V

8 50~641 EC₅₀

125Nm~3461nM

HIV

3309

90% 10

26%~96%

10 [26% 34% 46%

57% 59% 64% 70% 96%]

/

NNRTI

CCR5

Ames

Ames

1 3

1.6 3.8

1.2

1000mg/kg

GD6~15

1000mg/kg

GD7~19

1000mg/kg

GD8~20

AUC

3

1

1000 mg/kg

50%

AUC

150 mg

1

4

AUC

150 mg

1

1.2

2

800/100 mg / 800/150 mg

37%

3~4.5 2~5

1.7

95% 1-

97%~98%

2

P450 CYP3A ¹⁴C-

/ 400/100 mg

3 HIV-1

¹⁴C- CYP3A CYP2D6

99%

CYP3A

¹⁴C- / 400/100 mg ¹⁴C-

79.5% 13.9%

41.2% 7.7% 150 mg

32.8 L/h 5.9 L/h

11

¹⁴C- 86%

8.2% 3~4 .

17

65

HIV

HIV-1 18~75 65

. 65

HIV

16.8%

¹⁴C- /

7.7%

30~60 mL/ n=20. HIV CrCl

. CrCl <30 mL/ HIV-1

600/100 mg

Child-Pugh A n=8.

Child-Pugh B n=8

55% Child-Pugh A 100% Child-Pugh B

/

Child-Pugh

B HIV-1

Child-Pugh C

PK

/

2 3 3 1

6-12 12

C_{max} AUC_{24h}

12 2 3 / 800/150 mg q.d.

	2 ± SD	3 N=7	3 N=6 N=6
C _{max} ng/mL		4340 ± 1616	4910 ± 970	7918 ± 2199
AUC _{24h} ng.h/mL		47293 ± 19058	47991 ± 9879	99613 ± 34862
C _{min} ng/mL		168 ± 149	184 ± 99	1538 ± 1344

2 C_{max} AUC_{24h} C_{min}

49% 56% 92% 3 37% 50% 89%

30

30 /

24

JX20170271

H20180030

Janssen-Cilag International N.V.

Turnhoutseweg 30, B-2340 Beerse, Belgium

Janssen-Cilag International N.V.

Turnhoutseweg 30, B-2340 Beerse, Belgium

Janssen Ortho, LLC

State Road 933, KM 0.1, Mamey Ward, Gurabo, Puerto Rico, 00778, United

States of America

Janssen-Cilag SpA

Via C. Janssen, Borgo San Michele, 04100 Latina, Italy

19

710304

400 888 9988

029 82576616

<http://www.xian-janssen.com.cn>