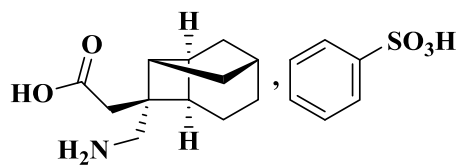


Crisugabalin Besilate Capsules

Benhuangsuan Kelijiabalin Jiaonang

2-[(1R,2R,3R,6R,8R)-2-(4-sulfamoylphenyl)propyl]piperidine-3-carboxylic acid [4.2.1.0^{3,8}] -2-]



$C_{12}H_{19}NO_2 \cdot C_6H_6O_3S$

367.46

20mg $C_{12}H_{19}NO_2$

20mg 2
65
1 40mg
2
20mg 40mg 2

1/2 1/4

65 65
585
327
457 6 274
12

178
40mg/ 20mg bid 180

1%
40.4% 18.8%

21(11.8)	42(23.3)	7 (4.0)
6 (3.4)	11 (6.1)	1 (0.6)
10 (5.6)	5 (2.8)	4 (2.3)

(SOC)	(%)	
(PT)		
	82 (27.2)	96
	25 (8.3)	27
	9 (3.0)	11
	6 (2.0)	6
	3 (1.0)	3
	8 (2.7)	9
	3 (1.0)	3
	5 (1.7)	5
	4 (1.3)	4
	3 (1.0)	3
	4 (1.3)	4

0.7%

	123	40mg/
20mg bid	122	80mg/ 40mg bid
	1%	3
42.9%	29.0%	

(((
(((
(((
3 (2.4)	9 (7.4)	1 (0.8)
5 (4.1)	2 (1.6)	1 (0.8)
5 (4.1)	29 (23.8)	3 (2.4)

	4 (3.3)	12 (9.8)	0
	4 (3.3)	8 (6.6)	6 (4.8)
	4 (3.3)	5 (4.1)	4 (3.2)
	3 (2.4)	3 (2.5)	0
	2 (1.6)	4 (3.3)	0
	0	5 (4.1)	0
	1 (0.8)	3 (2.5)	1 (0.8)
	3 (2.4)	2 (1.6)	0
	1 (0.8)	3 (2.5)	0
	3 (2.4)	3 (2.5)	0

		2.0%	0%	2
1	0.8%	40mg bid		
				/
	22.7%	5.7%		7.5%
0.3%	79.5%			20.5%
	5		3	
				/

4.0% 1.6% 7% /

1.7% 0.8% /

1 0.6% 40mg bid

1.5% 0.3% /

6 2.0% 20mg bid 4 1.3% 40mg bid
3
2

/

18

252 65 eGFR 60 mL/min/1.73 m²

n=145

n=107

65

65

<65 n=448

65 n=232

7.35 ~ 25.2%

CYP

CYP1A2 2B6 2C8 2C9 2C19 2D6 3A4

CYP1A

2 CYP2B6 CYP3A4

O

ATP1B1 OATP1B3 OATP2B1 OAT1 OATP1A2 MATE1 MATE2-K P-gp

BCRP OAT3 OCT2 P-gp BCRP OATP1B1 OAT

P1B3 OATP2B1 OAT1 OATP1A2 MATE1 MATE2-K OAT3 OCT2

OAT3

OCT2

4-1

4-2

PK	n=23		n=23		GMR (90%CI)
	Mean	SD	Mean	SD	
C _{max} (ng/mL)	611	(173)	721	(162)	1.20 (111.26%, 128.48%)
AUC _{0-t} (h*ng/mL)	3190	(602)	4570	(936)	1.43 (138.31%, 148.10%)
AUC _{0-∞} (h*ng/mL)	3250	(601)	4630	(931)	1.42 (137.03%, 147.50%)

PK	n=24		n=24		GMR (90%CI)
	Mean	SD	Mean	SD	
C _{max} (ng/mL)	617	(154)	687	(166)	1.12 (104.23%, 119.45%)
AUC _{0-t} (h*ng/mL)	3520	(758)	5680	(1100)	1.62 (156.66%, 167.45%)
AUC _{0-∞} (h*ng/mL)	3570	(762)	5730	(1100)	1.61 (155.91%, 166.79%)

5

PK	n=21		n=21		GMR (90%CI)
	Mean	SD	Mean	SD	
C _{max,ss} (ng/mL)	1320	(308)	1070	(269)	0.81 (76%, 87%)
AUC _{0-tau,ss} (h*ng/mL)	7350	(1100)	6190	(1430)	1.12 (79%, 87%)

:C_{max,ss}AUC_{0-tau,ss}

0

-

_____ 5~120 mg
 1.33~1.67h
 h AUC_{0-t} T_{max} 3.96 h v.s. 1.37
 C_{max} 33.96%

0.9 400 2000 10000 ng/mL
 2.7% 5~120 mg V_z/F 67~133L
 2.8% 3.3%

CYP450

CYP CYP1A2 2B6 2C8 2C9 2C19 2D6 3A4
 CYP1A2 CYP2B6 CYP3A4
 OATP1B1 OATP1B3 OATP2B1 OAT1 OATP1A2 MATE1 MATE2-
 K P-gp BCRP OAT3 OCT2

2%
 5~120mg CL/F 10.6~13.8L/hr
 3.68~6.42 h

40mg 79.21%
6.55%

n=74 n=606
6.57~10.1%

n=8 20 mg 90 GFR<130 mL/min,
60 GFR<90 mL/min, n=8 30 GFR<60 mL/min
n=8 15 GFR<30 mL/min, n=8
C_{max} 6.00% 13.83% 21.63% AUC₀₋ 14.63% 119.57%
272.61%

1/2 1/4

PK

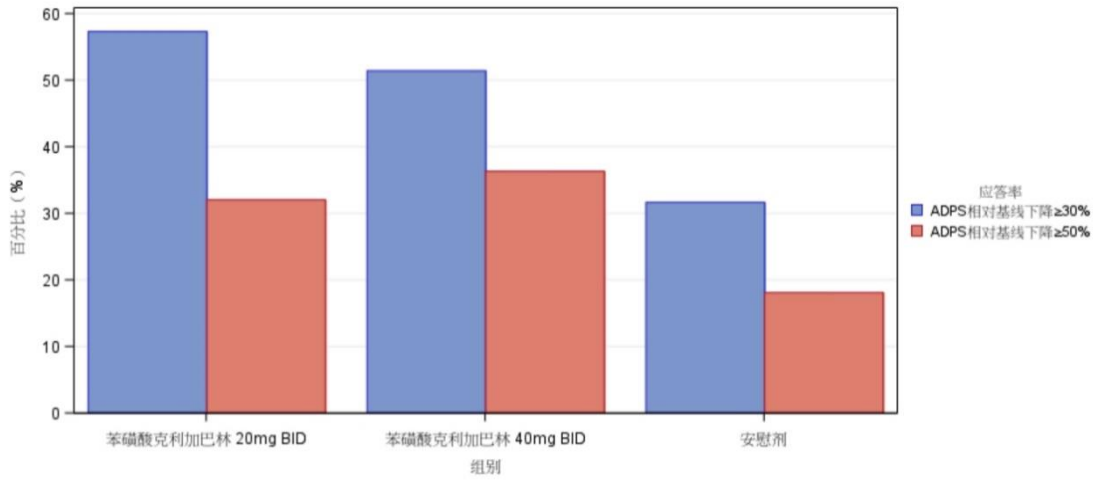
PK

18-75

6 HbA1c 9.0% 30
VAS 40 mm < 90 mm

20mg bid 40mg bid 60mg bid 80mg bid

		300mg/							13
		20mg bid	40mg bid						
								1:1:1	
		20mg bid	40mg bid						13
				13	ADPS				
				20mg bid	40mg bid			13	ADPS
						-2.24 (1.550)	-2.16 (1.785)	-1.23 (1.681)	
13	ADPS		30%				102	57.3%	92
	51.4%	56	31.6%	13	ADPS			50%	
	57	32.0%	65	36.3%	32	18.1%		40mg/	20mg
bid	80mg/	40mg bid				p<0.0001	1	2	
		13	DSIS						VAS



2 13 ADPS

52 40mg bid
40mg bid
20mg bid

52 VAS 301 43
52 VAS -23.4±19.38 2-

52 VAS

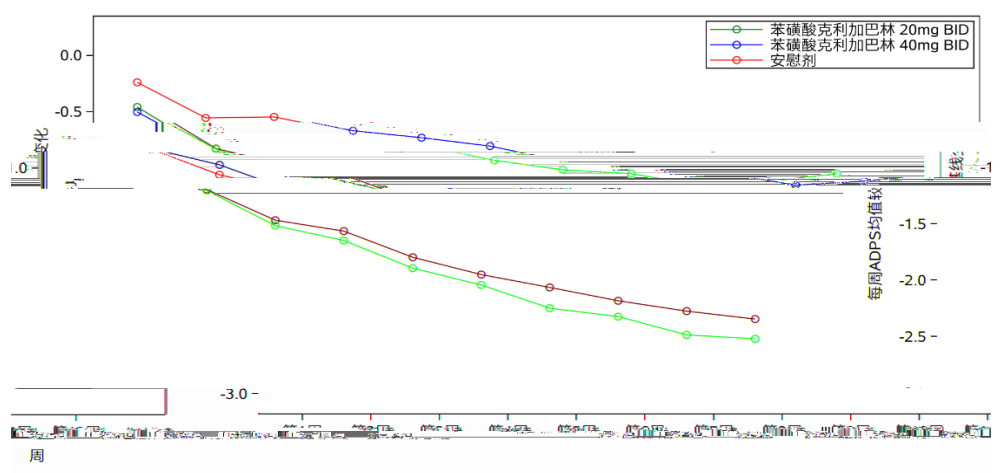
18 1 VAS 40 mm

1:1:1 20mg bid 40mg bid
12 12 ADPS
20mg bid 40mg bid
-2.513 (2.0055) -1.047 (2.0308) 40mg bid ADPS
-2.338 (1.6615)
95% CI -1.498 -1.983 -1.013 p<0.001 20mg bid
ADPS 95% CI -1.140 -1.631 -0.649

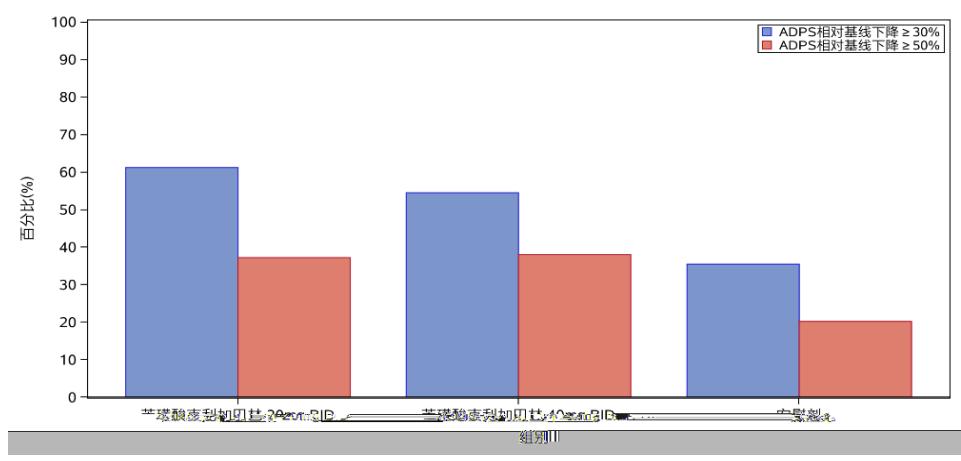
p<0.001 3 20mg bid 40mg bid
 12 ADPS 30% 74 61.2% 66
 (54.5%) 44 (35.5%) 12 ADPS 50%
 45 (37.2%) 46 (38.0%) 25 (20.2%) 4

12
 14

80mg/ 40mg bid
 264 71.0%
 26 VAS -39.09 19.590



3 ADPS



4 12 ADPS

-	GABA			GABA _A	GABA _B
				[³ H]	
		Ames	CHL		
					4
		2	7		15 60
240mg/kg/	[MRHD	80mg/ 1.8
7.3 29]	240mg/kg/				
			240mg/kg/		
	60 mg/kg/			240mg/kg/	
-					6~17
		5 20	100mg/kg/	100 mg/kg/	
			-		100mg/kg/
	AUC		MRHD	37	
-					6~18
		5 20	80mg/kg/	80mg/kg/	-
					-
	20mg/kg/		AUC	MRHD	3.4
				6	21
	5 20	100mg/kg/	100 mg/kg/		
				20mg/kg/	AUC
MRHD	5.2			100 mg/kg/	AUC
	MRHD	33			

SD 104 20 60
200 mg/kg/ 200mg/kg/ MRHD 101
140 AUC rasH2 26
6 100 400 1500 mg/kg/
1500 mg/kg/ MRHD 216 265
AUC

25

/ /

9 / 6

/

24

YBH08292024

H20240018

17

856000

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