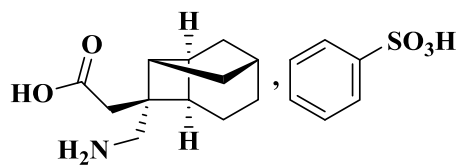


Crisugabalin Besilate Capsules

Benhuangsuan Kelijiabalin Jiaonang

2-[(1R,2R,3R,6R,8R)-2-(4-sulfamoylphenyl)propyl]piperidine-3-carboxylic acid [4.2.1.0<sup>3,8</sup>] -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



(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 3
1%		
42.9%	29.0%	

( ) (□)	( ) (□)	( ) (□)
( 5) !	0( 5) !	5) !
( %)	( %)	( %)
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 m<sup>2</sup>

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 <sub>max</sub> (ng/mL)	611	(173)	721	(162)	1.20 (111.26%, 128.48%)
AUC <sub>0-t</sub> (h*ng/mL)	3190	(602)	4570	(936)	1.43 (138.31%, 148.10%)
AUC <sub>0-∞</sub> (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 <sub>max</sub> (ng/mL)	617	(154)	687	(166)	1.12 (104.23%, 119.45%)
AUC <sub>0-t</sub> (h*ng/mL)	3520	(758)	5680	(1100)	1.62 (156.66%, 167.45%)
AUC <sub>0-∞</sub> (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 <sub>max,ss</sub> (ng/mL)	1320	(308)	1070	(269)	0.81 (76%, 87%)
AUC <sub>0-tau,ss</sub> (h*ng/mL)	7350	(1100)	6190	(1430)	1.12 (79%, 87%)

:C<sub>max,ss</sub>AUC<sub>0-tau,ss</sub>

0

-



\_\_\_\_\_ 5~120 mg  
 1.33~1.67h  
 h AUC<sub>0-t</sub> T<sub>max</sub> 3.96 h v.s. 1.37  
 C<sub>max</sub> 33.96%

0.9 400 2000 10000 ng/mL  
 2.7% 5~120 mg V<sub>z</sub>/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<sub>max</sub> 6.00% 13.83% 21.63% AUC<sub>0-</sub> 14.63% 119.57%  
272.61%

1/2 1/4

PK

PK

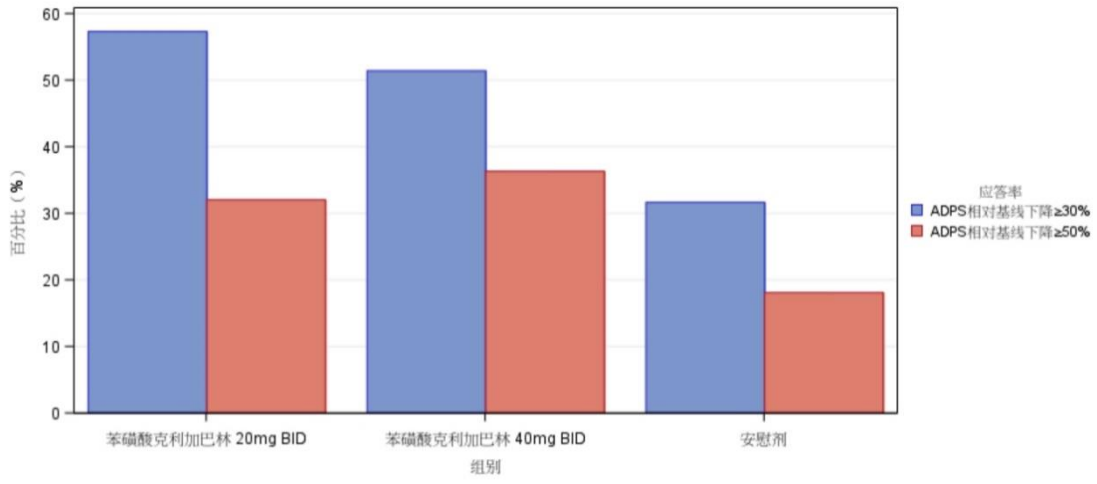
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18-75

6 HbA1c 9.0% 30  
VAS 40 mm < 90 mm

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





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



-	GABA			GABA <sub>A</sub>	GABA <sub>B</sub>
				[ <sup>3</sup> 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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