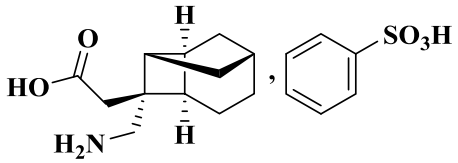
Crisugabalin Besilate Capsules

Benhuangsuan Kelijiabalin Jiaonang

2-[(1*S*,2*S*,3*R*,6*S*,8*S*)-2-( ) [4.2.1.$0^{3,8}$] -2-]



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

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 80mg/ 40mg bid 1

≥1%

40.4% 18.8%

1 **≥1.0%**

	40mg (N =178)	**80mg (N =180)**	**(N =176)**
	%	**%**	**%**
	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)
	4 (2.2)	4 (2.2)	4 (2.3)
	2 (1.1)	0	2 (1.1)
	3 (1.7)	1 (0.6)	1 (0.6)
	3 (1.7)	4 (2.2)	1 (0.6)
	0	5 (2.8)	1 (0.6)
	3 (1.7)	1 (0.6)	1 (0.6)
	3 (1.7)	4 (2.2)	2 (1.1)
	2 (1.1)	2 (1.1)	1 (0.6)

5.1% 1.1%

3.7%

1.0% 0.5%

≥2 0.8%

0.4% 0.4%

52

283 6 273

1 2 ≥1%

2 **≥1.0%**

(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%

3 **≥ 1.0%**

	40mg (N =123)	**80mg (N =122)**	**(N =124)**
	(%)	(%)	(%)
	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

/

≥7%

4.0% 1.6% /

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^2

n=145 n=107

65

65

<65 n=448

≥65 n=232 7.35～25.2%

CYP

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

OAT3 OCT2

4-1 4-2

4-1		**PK**	
PK	n=23 Mean SD	n=23 Mean SD	GMR (90%CI)
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%)
$AUC_{0-\infty}$ (h*ng/mL)	3250 (601)	4630 (931)	1.42 (137.03%, 147.50%)

4-2		**PK**	
PK	n=24 Mean SD	n=24 Mean SD	GMR (90%CI)
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%)
$AUC_{0-\infty}$(h*ng/mL)	3570 (762)	5730 (1100)	1.61 (155.91%, 166.79%)

5

5		**PK**	
PK	n=21 Mean SD	n=21 Mean SD	GMR (90%CI)
$C_{max,ss}$(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 -

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