

2007 02 08
2008 03 21
2008 09 09
2009 05 12
2011 02 28
2011 05 17
2012 05 21
2014 11 21
2015 11 02
2016 05 11
2017 04 26
2018 05 22
2018 07 11
2019 02 26
2019 05 22
2019 05 28
2020 03 02
2020 05 15

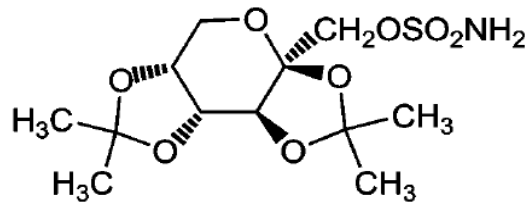
托吡酯片说明书

®

Topiramate Tablets

Tuobizhi Pian

2, 3, 4, 5- - (1-)-β-D-



$C_{12}H_{21}NO_8S$

339.36

25mg: 101

100mg: 101

2~16

(1) 25mg (2)100mg

17

25~50mg

1

Add MAH information into label

1 2 25~50mg 100mg / 2
1
200mg 200mg
200~400mg 2 1600mg/

25mg 5~9mg/kg/ 2
1~3mg/kg/ 1 1 2
1~3mg/kg/

(CL_{CR}<70ml/)

2

4111	3182	929	34	20	2847
<hr/>					
1					1%
	200~400mg/		5%		

/	200~400mg/ (N=354) %	600~1000mg/ (N=437) %	(N=382) %
	5.4	6.2	1.8
	5.1	8.7	3.7
	8.2	19.5	3.1
	4.5	9.4	1.6
	3.1	5.0	0.8
	3.1	11.7	3.4
	3.1	6.4	4.5
	2.8	3.2	1.8
	1.7	2.3	1.3
	1.7	2.1	0.5
	1.7	6.6	2.9
	1.7	3.2	1.0
	1.7	4.6	1.0
	17.8	17.4	8.4
	16.4	34.1	13.6
	8.2	17.2	3.7
	7.1	11.4	4.2
	6.2	11.7	6.8
	5.6	8.0	2.1
	5.4	6.2	1.0
	5.1	10.8	1.8
	4.5	11.9	1.8
	4.0	9.4	5.0
	3.4	5.3	1.0
	3.4	3.9	2.4
	3.1	5.9	1.0
	3.1	4.8	2.9
	1.4	4.3	0.8
	1.4	5.0	1.3
	1.1	2.7	0.5
	7.3	12.1	5.0
	5.4	8.9	2.4
	2.0	1.4	0.3

Add MAH information into label

1

1%

/	200~400mg/ (N=354) %	600~1000mg/ (N=437) %	(N=382) %
	6.8	15.1	8.4
	5.1	14.0	5.2
	3.7	3.9	2.1
	3.7	3.2	1.8
	3.1	3.2	1.3
	2.3	3.0	2.1
	1.7	3.7	0.3
	1.1	2.7	0.8
	2.0	2.5	1.3
	1.7	2.1	0.8
	1.1	1.8	0.3
	13.0	30.7	11.8
	9.3	14.6	3.7
	3.4	3.0	1.8
	1.4	2.5	1.3
	9.0	11.9	4.2
	200~400mg/		

-

2

(2~16)

2%

5~9mg/kg/

5%

2

2%

/	(N=104) %	(N=102) %
	19.2	12.7
	5.8	1.0
	8.7	6.9
	5.8	3.9
	2.9	2.0
	2.9	2.0
	15.4	6.9
	13.5	8.8
	10.6	2.0
	5.8	2.0
	4.8	2.9
	3.8	1.0
	4.8	1.0
	5.8	4.9
	6.7	5.9
	16.3	4.9
	11.5	8.8
	4.8	2.0
	9.6	1.0
2~16	5~9 mg/kg/	

-

3

1%

400mg/

5%

3

1%

/	50mg/ (N=257) %	400mg/ (N=153) %
	0.8	2.0
	3.5	12.4
	2.3	2.6
	4.3	8.5
	3.9	6.5
	2.3	4.6
	3.5	4.6
	0.8	2.6
	0.4	2.0
	1.6	2.0
	18.7	40.5
	1.2	7.2
	2.3	5.9
	4.3	5.2
	1.6	3.3
	1.6	2.6
	0.4	2.0
	1.2	2.0
	0.8	2.0
	0	2.0
	0	1.3
	0.4	1.3
	0	1.3
	0	1.3
	1.6	1.3
	1.2	2.0
	0	1.3
	5.4	6.5
	1.2	3.3

Add MAH information into label

3

1%

/	50mg/ (N=257) %	400mg/ (N=153) %
	0.4	2.6
	0.8	2.6
	1.2	2.0
	0.4	2.0
	0	1.3
	0.4	3.9
	1.6	3.3
	0.4	3.3
	0.4	2.0
	0	1.3
	2.7	3.3
	1.9	2.0
	0.4	1.3
	0	2.6
	0.8	2.0
	0.8	2.0
	0.8	1.3
	15.2	14.4
	3.5	5.9
	3.1	3.3
	7.0	17.0
400mg/		

-

4

10~16

≥2%

400mg/

5%

4

2%

/	50mg/ (N=77) %	400mg/ (N=63) %
	1.3	4.8
	0	4.8
	1.3	4.8
	0	3.2
	3.9	15.9
	3.9	7.9
	0	3.2
	0	3.2
	3.9	9.5
	3.9	4.8
	0	6.3
	0	6.3
	0	4.8
	7.8	20.6
	0	3.2
10	400mg/	

5

1%

Add MAH information into label

6

2%

7

$\geq 1/10$

$\geq 1/100$ < $1/10$

$\geq 1/1000$ < $1/100$

$\geq 1/10000$ < $1/1000$

< $1/10000$

/

1

40

400mg

6mg/kg/

4mEq/L

Add MAH information into label

10mEq/L

/

/

Z

Z

			400mg/		
			<20mEq/L	32%	1%
50mg/				400mg/	
		<17mEq/L		>5mEq/L	3%
	0%	≥16		50mg/	
			14%	400mg/	25%
			<17mEq/L		>5mEq/L
50mg/	1%	400mg/	6%		400mg/

Lennox-Gastaut

2~16

6mg/kg/

67%

10%

<17mEq/L

>5mEq/L

11%

Add MAH information into label

0% 5

5mg/kg/

2

25mg/kg/ -

-5.9mEq/L <20mEq/L

0% 5mg/kg/ 30% 15mg/kg/ 50% 25mg/kg/

45% <17mEq/L ≥20mEq/L >5mEq/L

0% 5mg/kg/ 4% 15mg/kg/ 5%

25mg/kg/ 5%

6~15

50mg/ 9% 400mg/ 25%

<17mEq/L

>5mEq/L 50mg/ 1% 400mg/ 6%

AED

AED

/

11 AED 199

AED

2 1.8 95% CI 1.2 2.7 12 27863

AED 0.43% 16029

0.24% 530 1

4

1 AED

Add MAH information into label

24
24
AED
AED
5~100
8
AED
1000
1000
/

						100~200mg/
				200mg/	42%	400mg/
41%	600mg/	52%	800mg/	1000mg/	56%	
14%						
50mg/	19%	400mg/	26%			
/						
	/					
/						
		200mg/	1000mg/			
		400mg/				
50mg/	400mg/			50mg/	9%	400mg/
15%				14%		
						/
						/
/						
				50mg/		400mg/
	50mg/	1	2%	400mg/	7	12%
						/

Add MAH information into label

400mg/

/

2796

10

0.0035

0.0005

0.003

0.005

/

1~24

8% 5mg/kg/

10%

15mg/kg/

0%

25mg/kg/

9%

≥50%

2

/

2

/

/

/ 1~24

0%	5mg/kg/	12%	15mg/kg/	7%	25mg/kg/	17%		
/						5mg/kg/	0%	
15mg/kg/		7%	25mg/kg/	8%				

Add MAH information into label

35°C

6%

2%

0.4%

0.1%

3%

1%

2

BUN

/

18.

AED

19.

Stevens-Johnson

SJS

TEN ()

SJS TEN

SJS TEN

/

AED
 AED
 <2500
 SGA
 SGA
 SGA
 3
 SGA
 NAAED
 1.2%
 0.39%~0.46%
 AED
 AED
 0.12%
 CDC
 0.17%
 NAAED
 9.6 95%
 =3.6~25.7
 UK
 3.2%
 16
 0.2%

/

5

10~20%

2

Lennox-Gastaut

1 24

20

5 15 25mg/

/ 1 24

/

/

/

/

12%

0%

40%

16%

3%

3% 7%

5%

0%

3%

0%

34%

6%

Add MAH information into label

7% 0% 25mg/kg/ 5%
0%
5mg/kg/ 10% 15mg/kg/ 9% 25mg/kg/ 14%
11% 6%

Z

37 /1000

1 24

2

15%

CYP2C19

100mg 400mg

Add MAH information into label

327mg

	**	(48%)
CBZ		(40%)
		NS
		NS
**		
NS		

AUC 12%

(1mg /35µg

50~200mg/

AUC

200 400 800mg/

AUC

18% 21% 30%

50~800mg/

AUC

200~800mg/

AUC

50~200mg/

Add MAH information into label

200mg/
 200mg/
 600mg/ AUC 26%
 100 250 400mg/
 1~6mg/ AUC 250mg/ 400mg/
 AUC 16% 33% 9- AUC
 9- AUC
 25mg 2 96mg
 C_{max} 27% AUC
 29%
 C_{max} AUC_{0-12h} 18% 25% CL/F
 20% T_{max}

Add MAH information into label

						AUC	15%	C _{max}
							C _{max}	AUC
13%	16%				C _{max}	AUC	60%	
				5mg/		150mg/	2	
						AUC ₂₄	25%	
	4- - -		M1	3- -		M2		13%
15%								

35°C

K

/

PT/INR

K

INR

	a%	a%
	C _{max} AUC 20%	NS
	AUC 31%	NS
4-	C _{max} 17% 2 50mg	C _{max} 9% 16% AUC 9% 17% 2 40mg 80mg
		NS

AUC 25%
AU1.9 Tm C₁ Tm C₂

6

2~16

4

EPMN-106 487 6~83 6

50mg/ 400mg/ 6

Kaplan-Meier 400mg/ 50mg/ p=0.0002 Log

Rank

p 0.046

100mg/ Kaplan-Meier 6

82.9% 71.4%

p=0.005 75.7% 58.8% p=0.001

0.516 95% 0.364~0.733)

AED

YI 15~63 48

100mg/ 1000mg/

54% 17%

p=0.005

p=0.002 ≤0.002

EPMN-104 6~85 252

25 50mg/ 200 500mg/

Add MAH information into label

	54%		39%		p=0.022
		3			
	p=0.015				
EPMN-105		6~84	613	100mg/	
200mg/				95%	
	0				
YI EPMN-104		320	32	16	
		2~5			
6					
				2	
	4~12				
	12	12	12	8	8
					4
3					
			5		100mg
		100	200mg/		
		119		25	50mg/
	25	50mg/			
			200mg/		
4	8	12			
			11		

1

2 AED

8 AED

6

AED

25 50mg

25mg 150mg/

125 175 225 400mg/

6mg/kg

8

		a	mg/				
			200	400	600	800	1,000
YD		42	42	40	41		
		5.9	200	390	556		
		6.0	200	400	600		
YE		44			40	45	40
		9.7			544	739	796
		10.0			600	800	1,000
Y1		23		19			
		3.8		395			
		4.0		400			
Y2		30			28		
		5.7			522		
		6.0			600		
Y3		28				25	
		7.9				568	
		8.0				600	
119		90	157				
		8	200				
		8	200				
a			Y1 4 /	YD Y2 6 /			
b	Y3 8 /	YE 10 /					

50%

			mg/						6mg/kg/ *
			200	400	600	800	1,000		
YD		45	45	45	46				
		11.6	27.2 ^a	47.5 ^b	44.7 ^c				
		18	24	44 ^d	46 ^d				
YE		47			48	48	47		
		1.7			40.8 ^c	41.0 ^c	36.0 ^c		
		9			40 ^c	41 ^c	36 ^d		
Y1		24		23					
		1.1		40.7 ^e					
		8		35 ^d					
Y2		30			30				
		-12.2			46.4 ^f				
		10			47 ^c				
Y3		28				28			
		-20.6				24.3 ^c			
		0				43 ^c			
119		91	168						
		20.0	44.2 ^c						
		24	45 ^c						
YP		45						41	
		10.5						33.1 ^d	
		20						39	
		^a p=0.080	^b p 0.010	^c p 0.001					
		^d p 0.050	^e p=0.065	^f p 0.005					
*	YP	<9.3mg/kg/			6mg/kg				
	125 175 225 400mg/	mg/							

Add MAH information into label

GABA

GABA_A

GABA_A

Kai nate

Kai nate/AMPA - -3- -5- -4- N- -D-

NMDA NMDA 1μ M-200μ M

1μ M-10μ M

MES

SER

GABA_A

Ames

DNA

100mg/kg [mg/m²

RHD 400mg/

2. 5

20 100 500mg/kg mg/m²

RHD 0.2 500mg/kg

Add MAH information into label

				20	100	500mg/kg		0.2	2.5	30	400mg/kg
400mg/kg	mg/m ²		RHD	10							
				20mg/kg		mg/m ²			RHD		0.5
										400mg/kg	
				100mg/kg							
				20	60	180mg/kg		10	35	120mg/kg	35mg/kg
mg/m ²		RHD	2				/				120mg/kg
mg/m ²		RHD	6								
35mg/kg										/	
								0.2	4	20	100mg/kg
200mg/kg	200mg/kg	mg/m ²		RHD	5						2
	2mg/kg	mg/m ²		RHD	0.05						20
						100mg/kg					/
										0.2	2.5
										30	
400mg/kg		400mg/kg	mg/m ²				RHD		10		
	30mg/kg	mg/m ²		RHD	1						
				20	75	300mg/kg					21
300mg/kg											
										300mg/kg	
							RHD	400mg			0.5~1
	400mg									1.5~2	
								120mg/kg	mg/m ²		
RHD	3										
											2
				12	50			30	90	300mg/kg	mg/m ²
						9mg/kg		5	-8		

Add MAH information into label

				100mg	2~3	T _{max}
		C _{max}	1.5μg/ml			
100mg ¹⁴ C-			81%			
				13~17%		
		4μg/ml				
	100~1200mg			0.80~0.55L/kg		
			50%			
				20%		
		50%				
	6					
¹⁴ C-					3%	
		2				
					81%	66%
¹⁴ C-	4			50mg	2	100mg
		2		18ml/		17ml/
			20~30ml/			
	100~400mg					
				4~8		
	100mg	2		C _{max}	6.76μg/ml	50mg 100mg
	2				21	
100mg			t _{1/2}	30.19±5.01h	31.07±4.67h	

Add MAH information into label

100~400mg 2

CL_{cr}<70ml/

26%

mg/kg

60 / /

36

WS₁- (X-070)-2006Z-2018

25mg: H20020555

100mg: H20020557

19

4 17F

710304

4008889988

029 82576616

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