2019 09 05

2019 10 22

2020 03 09

2020 07 01

2020 08 28

2021 01 29

2022 08 02

2023 04 13

波生坦分散片说明书

11% **ULN 3**

ALT AST

1

>12

1 **>20**

1

>3xULN

≥2xULN

1 **2**

Copper T380A IUD **LNg20 IUS**

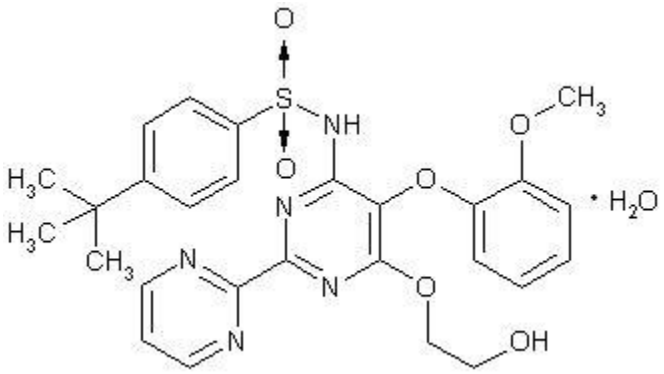
1

® Tracleer®

Bosentan Dispersible Tablets

Boshengtan Fensanpian

4- -N-[6-(2-)-5-(2-)-2-(2-)-4-]



$C_{27}H_{29}N_5O_6S \cdot H_2O$

569.63

“32”

PAH WHO 1

- ≥3 PAH PVR

12 18

- WHO II -IV PAH WHO 1
WHO II -IV
PAH 60% PAH 21%
PAH 18%

32mg $C_{27}H_{29}N_5O_6S$

1 **≤12**

≤12	**4** **4**
≥4-8kg	16mg/
>8-16kg	32mg/
>16-24kg	48mg/
>24-40kg	64mg/
>40kg	64mg/

12 **18** 12 18

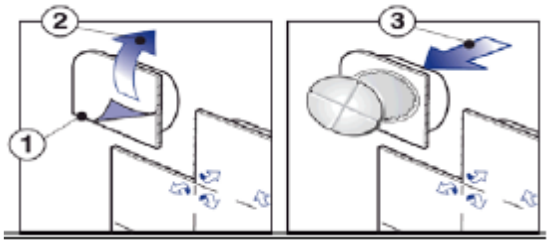
12 18

≤40kg 64mg/

12 18 >40kg PAH

64mg/ 4 128mg/

7



1.

2.

3.

≤40kg

64mg/ 40kg

64mg/ 4 128mg/

3

≥2

2 **3**

ALT/AST
> 3 ≤5×ULN 2
> 5 ≤8×ULN 2
> 8×ULN

3 **2**

3 ULN

10

1 1

36 10
1 1

3~7

20 2486
100mg–2000mg 1838 45
1% 0.5%
11.5% / 13.2% 10.9%
/ 9.9%

20 ≥1/10
≥1/100 <1/10 ≥1/1,000 <1/100 ≥1/10,000 <1/1,000
<1/10,000

3 20

		[1]
		[1]
		[1]
		[2]
		/ [1]
		[3]
		[1,4]
		[1]
		[1,4]
		[1,4]
		[1]
		/ [1]
		[1]
		[5]

[1]

[2] 9.9% 9.1%

[3] 11.5% 9.8%

[4]

[5] 13.2% 10.9%

BREATHE-3 n=19 10 [3~15] 2mg/kg 12 PAH BREATHE-3 21% 16%

PAH 100
32mg FUTURE 1/2 FUTURE 3/ 2mg/kg n=33 2mg/kg
n=31 4mg/kg n=36 6 3 1
15 1 2 79 2 12 71.8 0.4-258

PAH
PAH 69.0% vs 41.3%
71.8
17.4 25%
20% 17% 15% 13% 10% 10%
10% 2
21 2 6 3 1 /
9% 5%

PPHN FUTURE-4
13 2mg/kg 8
4.5 0.5-10 4.0 2.5-6.5
7
2 3 0 2 0

26

20
≥3 11.2% 2.4% ≥8
3.6% 0.4% ≥2
0.2% 5 0.3% 6

FUTURE 1/2 FUTURE 3/ 100 PAH
2% ≥3xULN

FUTURE-4 13 PPHN 2mg/kg
10 0.5-10.0 ≥3xULN
3

10g/dL 8.0% 3.9%

FUTURE 1/2 FUTURE 3/ 100 PAH
10.0% 10g/dL 8g/dL

FUTURE-4 13 PPHN 6

-
- 2
- / AST / ALT ULN 3 ULN 2
- A
-

AST ALT 26

A

12

1 20

≥2

AST / ALT 3xULN 2xULN

PAH 1.7%

4-12

1 3 **3**

“ ”

85mmHg

62.5mg

4 125mg 5

25 WHO III PAH 23 2

3 6 25%

50% 6 22

1 3 6 2

2

CYP3A4 CYP2C9

32mg 32mg 1.87
mg 32mg

≥60mg/kg/ mg/m^2
125mg 2 -
1500mg/kg/

-1

1

PPHN

65 65

P_{450}

P_{450} CYP2C9 CYP3A4
CYP2C9
CYP2C9
CYP3A4
CYP3A4
CYP2C9
CYP3A4 CYP2C9 CYP2C19

P_{450} CYP1A2 CYP2A6 CYP2B6 CYP2C8 CYP2C9
CYP2C19 CYP2D6 CYP2E1 CYP3A

-

A A
A 30
3~4
A CYP3A4
50%

A

40% 30%
CYP2C9 CYP3A4

31% 14%
56% 66%
CYP3A4

500mg 6 S- CYP2C9
R- CYP3A 29% 38%
INR

INR

INR

125mg 5 CYP3A4
β- 34% 46%
CYP3A4

62.5mg CYP3A4 6
2
CYP3A4
CYP2C9 CYP3A4

125mg CYP2C9 CYP3A4 7
58% 90%
CYP3A4

C_{max} AUC

125mg 80mg
AUC 63% AUC 50%

125mg 40mg
42% C_{max} 27% AUC
C_{max}

+
125mg + 400+100mg 9.5 3~4
48 9 5

CYP3A4 +
62.5mg
125mg

9.5

14% 17%

HIV

-

C_{max} 22% AUC 10%

-

2400mg

2000mg/ 2

500mg 1000mg A 30

1 10000mg

24

PAH

WHO -

32 AC-052-351 213 AC-052-352 BREATHE-1

2 WHO

PPH PAH BREATHE-1

2 125mg b.i.d. 250mg b.i.d. AC-052-351

125mg b.i.d.

/ 62.5mg

4 125mg 250mg

8 AC-052-351 12 BREATHE-1 6

AC-052-351 12

12 AC-052-351 16 BREATHE-1
28 6
75.9±31.0m 95%CL=12.5 139.2 t- ,
p=0.0205 44.2±11.6m 95%CL=21.4 67.0 Mann-Whitney U- , p=0.0002 62.5mg
b.i.d. 1 2 7

AC-052-351
12 PAP CI PVR RAP
PCWP

4 AC-052-351 12

PAP mmHg	n=20	n=10	n=20	n=10	-6.7*
	53.7±13.4	55.7±10.5	-1.6±5.1	5.1±8.8	
(L/min/m²)	n=20	n=10	n=20	n=10	1.02**
	2.35±0.73	2.48±10.33	0.50±0.46	-0.52±0.48	
PVR dyn.sec/cm⁵	n=19	n=10	n=19	n=10	-415**
	896±425	942±430	-223±245	191±235	
RAP mmHg	n=19	n=10	n=19	n=10	-6.2**
	9.7±5.6	9.9±4.13	-1.3±4.1	4.9±4.6	
PCWP mmHg	n=19	n=10	n=19	n=10	-3.8*
	9.3±2.4	8.3±3.4	0.1±3.6	3.9±5.6	

±SD

* $p<0.05$

** $p<0.001$

WHO Borg “ ” PAH
Borg WHO

AC-052-351 9 42.8% WHO
1 9.1% 2 18.1%
AC-052-352 BREATHE-1 213 92% WHO
8% 42.4% WHO
30.4%

1 Log-rank 28

5 *

	BREATHE-1		**AC-052-351**	
	125mg b.i.d. n=74	**n=69**	**125mg b.i.d. n=21**	**n=11**
[n(%)]	5 7% [a]	14 20%	0 0% [b]	3 27%
	1 1%	2 3%	0 0%	0 0%
PAH	3 4%	9 13%	0 0%	3 27%
PAH	3 4%	6 9%	0 0%	3 27%
[c]	2 3%	3 4%	0 0%	3 27%

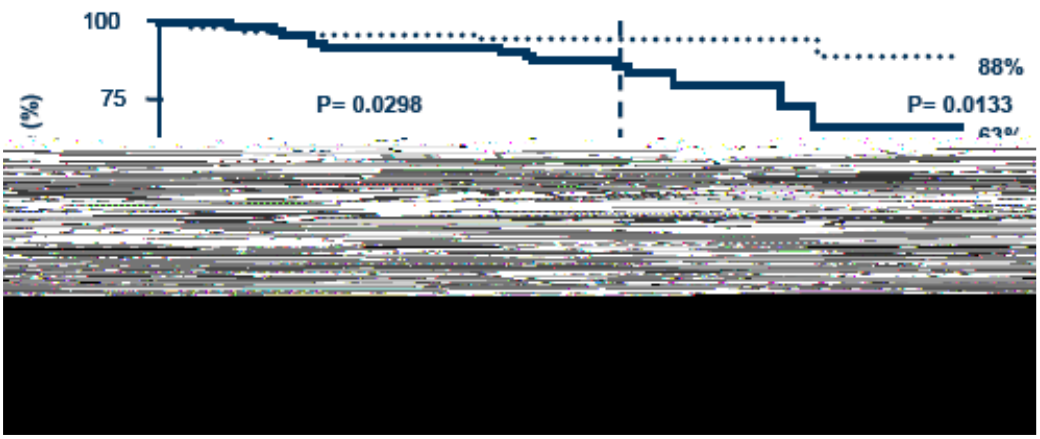
[a] Log-rank p=0.015

[b] Fish p=0.033

[c]

* PAH

1 BREATHE-1 28



BREATHE-1 Kaplan-Meier

n=74 n=69 16

n=19 n=13 28

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125mg AUC CV% 3496 49
5428 79 6124 27 ng·h/mL 125mg PAH
8149 47 ng·h/mL 10-20kg 20-40kg >40kg
43% 67% 75%

AC-052-365 FUTURE-1 36 2-11 PAH
2mg/kg 4mg/kg AUC 2mg/kg
AUCτ 3577ng·h/mL 4mg/kg AUCτ 3371ng·h/mL
125mg

AC-052-373 FUTURE-3 2mg/kg
FUTURE-1 n=31 2mg/kg
8535ng·h/mL AUCτ 4268ng·h/mL CV 61% 3 2
7879ng·h/mL AUCτ 3939ng·h/mL CV 72% 3 1
n=2 AUCτ 5914ng·h/mL CV 85% 1-2 n=7 AUCτ
3507ng·h/mL CV 70% 2 n=22 8820ng·h/mL AUCτ
4410ng·h/mL CV 58% 2mg/kg
7275ng·h/mL CV 83% n=27

BREATHE-3 FUTURE-1 FUTURE-3
2mg/kg
4mg/kg 2mg/kg

AC-052-391 FUTURE-4
AUC_{0-12} 164ng·h/mL n=11 AUCτ 6165ng·h/mL
CV 133% n=7 125mg / 0.6 PAH

65

Child-Pugh A
AUC 9% Ro 48-5033
AUC 33%

Child-Pugh B Ro
48-5033 5 Child-Pugh B
3 PAH Child-Pugh B
AUC [95%CI] 360 [212-613]ng·h/mL 4.7

AUC [95%CI] 76.1 [9.07-638]ng·h/mL Ro 48-5033 AUC [95%CI] 106 [58.4-192]ng·h/mL 12.4 Ro 48-5033 AUC [95%CI] 8.57 [1.28-57.2]ng·h/mL

Child-Pugh B Ro 48-5033

Child-Pugh C

Child-Pugh B C

15-30mL/min 10% 2 3%

25℃

/ 56 /

36

JX20190159

H20190051

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Patheon Inc.

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