

2017 09 29

2020 05 09

2020 09 10

# 马昔腾坦片说明书

1

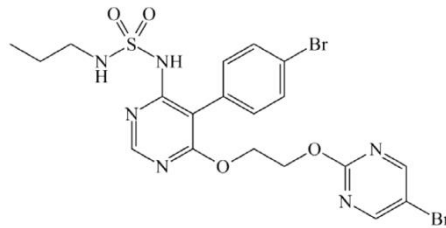
1

® OPSUMIT®

Macitentan Tablets

Maxitengtan Pian

N-[5-(4-bromophenyl)-6-[2-[(5-bromopyridin-2-yl)oxy]ethyl]amino]pyridin-2-yl]-N-propylsulfonamide



C<sub>19</sub>H<sub>20</sub>Br<sub>2</sub>N<sub>6</sub>O<sub>4</sub>S

588.27

“10”

ERA PAH WHO 1  
IV PAH PAH PAH  
6 PAH PAH PAH  
PAH WHO II -III PAH 2  
-5  
PAH 57% PAH 31%  
PAH 8%

10mg

10mg  
PAH

10mg

PAH

3 3 x ULN

PAH

[PAH

]

742

SERAPHIN

3.6

2

1

N=542

2

N=429

3

N=98

10 mg

11%

1

3%

1

	<b>10 mg</b> <b>(N=242)</b> <b>(%)</b>	<b>(N=249)</b> <b>(%)</b>
	13	3
/	20	13
	12	6
	14	9
	6	2
	9	6

ALT, AST

ERA

/

-

PH

[AST]  
ERA

[ALT]

ERAs

2

**2 SERAPHIN**

	<b>10 mg</b>	
--	--------------	--

4 15

	(N=242)	(N=249)
> 3 x	3.4%	4.5%
> 8 x	2.1%	0.4%

1.6% 10 mg 3.3%

3 [ULN]

2

PAH PAH ERA  
 PAH 10 mg  
 21.9% 20.5%

ERA

ERAs

1.0 g/dL 10 mg 18  
 10.0 g/dL 10 mg 8.7%  
 3.4%  
 5 15

**PVOD**

PVOD

ERAs

—

IUD

—

ERAs

14%

65

75

**CYP3A4**

CYP3A4

CYP3A4

**CYP3A4**

CYP3A4

HIV

CYP3A4

CYP3A4

HIV

CYP3A4

10mg

CYP

P-gp MDR-1

OATP1B1 OATP1B3

BSEP

NTCP

1

1

药物

马昔腾坦

活性代谢产物

推荐

西地那非

不需要调整剂量

7

15

环孢素 A

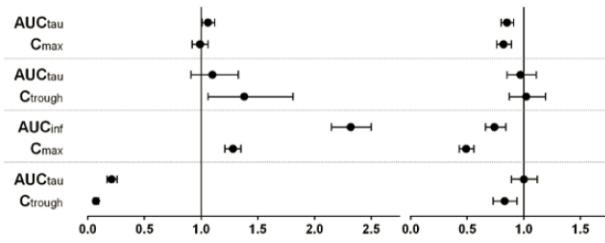
不需要调整剂量

酮康唑

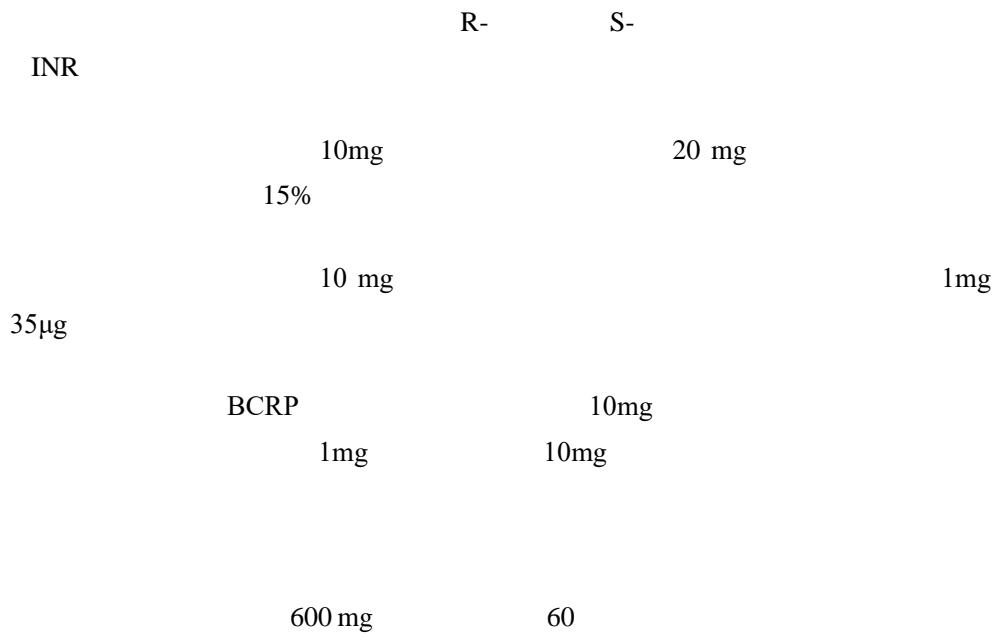
避免

利福平

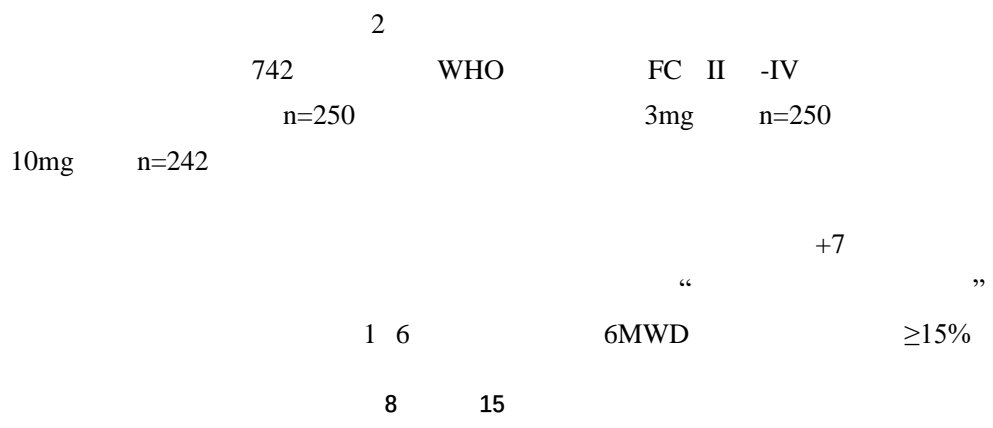
避免



CYP3A4



(PAH)





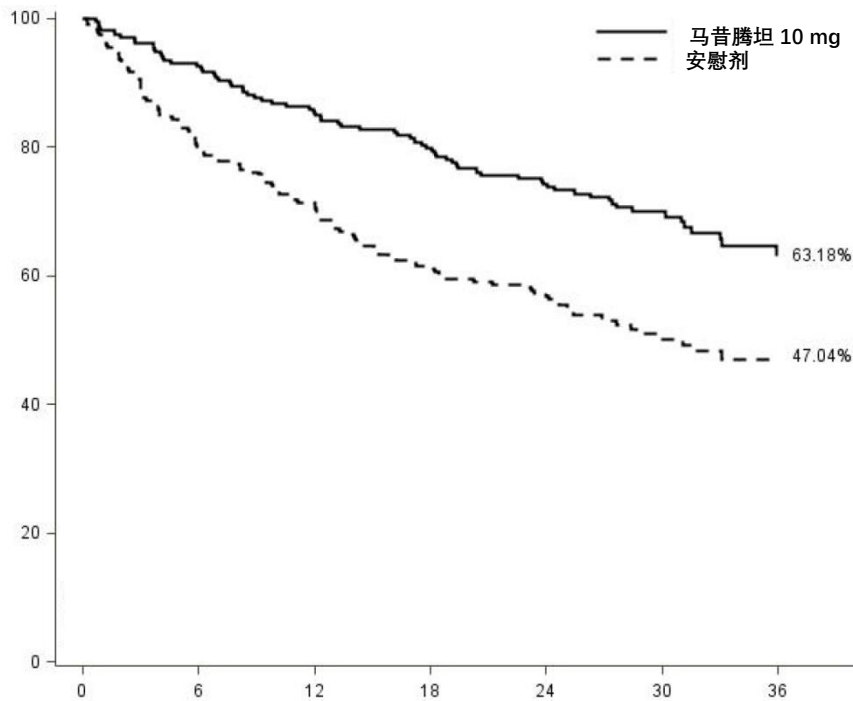
III IV  
 29% 46 14% 65 65 55%  
 77% 52% 46% 2% WHO II

31% 57% 8%  
 3% HIV 1%

61% / / 64% PAH 6%  
 10 mg 101 118  
 188 10 mg  
 45% HR 0.55 97.5% CI 0.39-0.76 p<0.0001 3 2 10 mg  
 6MWD PAH PAH

2 SERAPHIN

Kaplan-Meier



10 mg	242	208	187	171	155	91	41
	250	188	160	135	122	64	23

3

	<b>N=250</b> <b>n (%)</b>	<b>10 mg</b> <b>N=242</b> <b>n (%)</b>
*	116 (46.4)	76 (31.4)
/	93 (37.2) 17 (6.8) 6 (2.4)	59 (24.4) 16 (6.6) 1 (0.4)

\*

10 mg

3

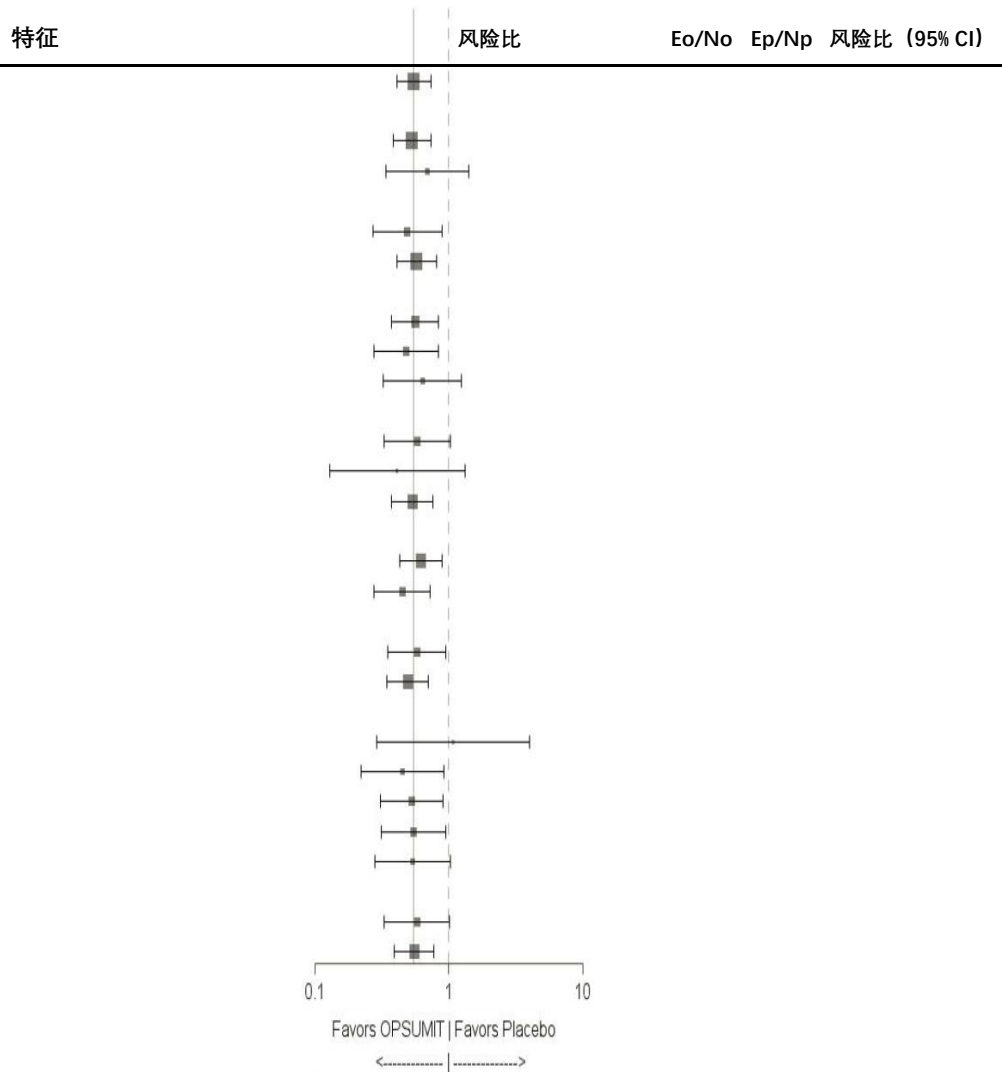
PAH

6MWD

WHO

10 mg

### 3 SERAPHIN



\*

6

7

18

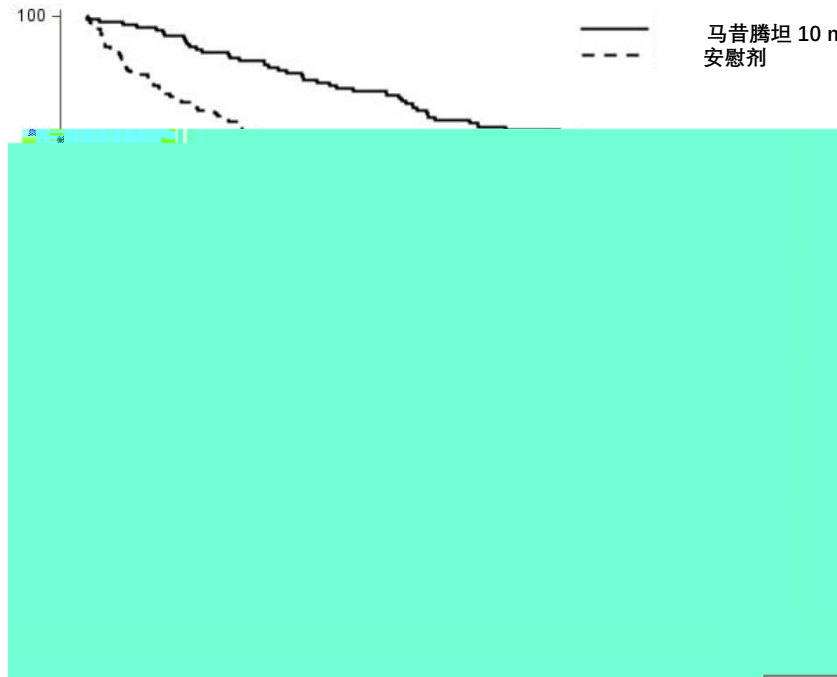
10

15

\*\* 1 WHO I  
 Eo= 10mg No= 10mg  
 Ep= Np=

PAH PAH 10 mg  
 PAH 50% HR 0.50 97.5% CI 0.34-0.75  
 p<0.0001 4 4

4 SERAPHIN PAH Kaplan-Meier  
 马昔腾坦 10 mg  
 安慰剂



10 mg 242 203 183 166 152 86 39  
 250 188 155 132 119 62 22

4 PAH PAH

		(N=250) n (%)	10 mg (N=242) n (%)
PAH	PAH	84 (33.6)	50 (20.7)
PAH	PAH	5 (2.0)	5 (2.1)
PAH	PAH	79 (31.6)	45 (18.6)

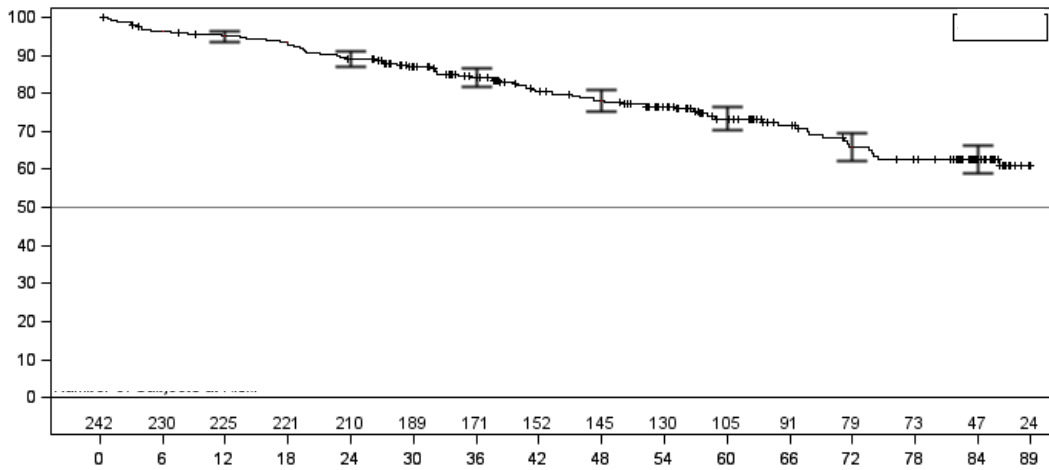
10 mg 6 6 6MWD

22 97.5% CI 3-41; p=0.0078 3 6MWD 6MWD  
 WHO WHO III/IV I/II  
 37 12 6MWD

10 mg 6 22% WHO 1  
 13%

N=242 10mg  
 1 2 3 4 5 6 7 Kaplan-Meier 95% 89%  
 84% 78% 73% 66% 63%[ 5] 4.6

**5 SERAPHIN** 2016 10 31  
 Kaplan-Meier 10 mg /



89 89 10%  
 AC-055-302 10mg

\*

-1 ET-1 ET<sub>A</sub> ET<sub>B</sub>  
 PAH ET

			ET-1	ET <sub>A</sub>	ET <sub>B</sub>	
	ET					20%
						6
		10 mg	N=57		N=67	
37%		95%CI 22-49			0.6 L/min/m <sup>2</sup>	95%CI 0.3-0.9

10mg	30mg	3	QTc
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		AUC
4~39		17
		12~116

Ames

	7	23
2		4
	19~44	

2

5

4 114

7

2

75 140

8.3 42

1mg-30mg

8

>99%

$\alpha$ -1-  
Vss/F

50L 40L

16 48

P450 (CYP) CYP3A4 CYP2C8 CYP2C9 CYP2C19

3

40%

50%

24%

CrCl 15-29 mL/min

14

15

30% 60%

Child-Pugh A B C

21% 34% 6%

20% 25%

25%

30

30 /

60

JX20190175

HJ20170376

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