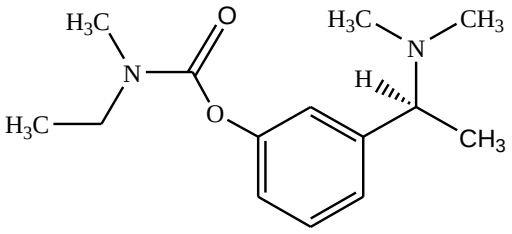
2020 06 02

外

Rivastigmine Transdermal Patch

Lisidiming Toupitieji

S -N- -N- -3-[1-( )]-



$C_{14}H_{22}N_2O_2$

250.34

[(2-) ,]

/ /

4.6mg/24

RIV-TDS 4.6mg/24h 9.5mg/24 RIV-TDS 9.5mg/24h

1 4.6mg/24 2 9.5mg/24

4.6mg/24	4.6mg/24	6.9mg	4.6cm^2
9.5mg/24	9.5mg/24	13.8mg	9.2cm^2

4.6mg/24

4 4.6mg/24
9.5mg/24

9.5mg/24

/
3
4.6mg/24

/

- / <6mg/ 4.6mg/24
- / 6-12mg/ 9.5mg/24

50kg

4.6mg/24 9.5mg/24 13.3mg/24
17.4mg/24 13.3mg/24 17.4mg/24
1
9.5mg/24
/ /
17.4mg/24 *
9.5mg/24
2

1 2
(1%~10% 1%) (0.1%~1% 0.1%) (0.01%~0.1%
0.01%) (<0.01%)

1 2687
4.6mg/24 9.5mg/24
13.3mg/24 * 17.4mg/24 * 24-48

**
*** *** *** ***

* 13.3mg/24
* 17.4mg/24
** 24
*** 24

/

2 24

(

2%)

	18 6.2	57 18.8	50 17.0	10 3.3	75 12.6
	18 6.2	31 10.2	16 5.4	10 3.3	49 8.2
	8 2.7	23 7.6	16 5.4	4 1.3	31 5.2
	7 2.4	21 6.9	22 7.5	7 2.3	28 4.7
	2 0.7	15 5.0	12 4.1	3 1.0	17 2.9
	10 3.4	13 4.3	18 6.1	5 1.7	23 3.9
	7 2.4	12 4.0	14 4.8	3 1.0	19 3.2
	11 3.8	12 4.0	13 4.4	4 1.3	23 3.9
	4 1.4	12 4.0	6 2.0	6 2.0	16 2.7
	7 2.4	11 3.6	4 1.4	2 0.7	18 3.0
	5 1.7	9 3.0	17 5.8	3 1.0	14 2.4
	9 3.1	8 2.6	5 1.7	4 1.3	17 2.9
	5 1.7	7 2.3	2 0.7	4 1.3	12 2.0

* 17.4mg/24

3

3%

	140 (56.7)	157 (62.5)
	27 (10.9)	7 (2.8)
	20 (8.1)	32 (12.7)
	19 (7.7)	31 (12.4)
	16 (6.5)	37 (14.7)
	15 (6.1)	25 (10.0)
	10 (4.0)	7 (2.8)
	10 (4.0)	17 (6.8)
	8 (3.2)	4 (1.6)
	6 (2.4)	11 (4.4)
	5 (2.0)	8 (3.2)

4.9% 8.4%

2.2% 3.7%

-

/

3 4.6mg/24

/

/

QT /

/

/

/

48

/

®

/ /

/

50kg

/

/

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/

/

/

/

88% 65 55% 75

/ P450

/

/

/

/ /

/

3.4 9

24

0.03mg/kg

13.3mg/24

24 48

24

10-20

24

ADAS-Cog -

ADCS-CGIC -

ADCS-ADL -

3 24

4

4 3 24

ITT-LOCF	9.5mg/24 N=251	® 12mg/ N=256	N=282
ADAS-Cog	n=248	n=253	n=281
	27.0±10.3	27.9±9.4	28.6±9.9
24	-0.6±6.4	-0.6±6.2	1.0±6.8
p	0.005*[1]	0.003*[1]	
ADCS-CGIC	n=248	n=253	n=278
	3.9±1.20	3.9±1.25	4.2±1.26
p	0.010*[2]	0.009*[2]	
ADCS-ADL	n=247	n=254	n=281
	50.1±16.3	49.3±15.8	49.2±16.0
24	-0.1±9.1	-0.5±9.5	-2.3±9.4
p	0.013*[1]	0.039*[1]	

* ITT LOCF

1 ADAS-Cog ADCS-ADL

2 CMH van Elteren ADCS-CGIC <4

24 5

ADAS-Cog 4 ADCS-CGIC ADCS-ADL

5 24

	%		
	9.5mg/24	® 12mg/	
ITT-LOCF	N=242	N=248	N=276
ADAS-Cog ADCS-CGI ADCS-ADL	17.4	19.0	10.5
p	0.037*	0.004*	

* p<0.05

9.5mg/24 12mg/

9.5mg/24

48

MMSE 10-24 24-48

9.5mg/24 13.3mg/24

9.5mg/24 48

MMSE

ADAS-Cog

- ADCS-IADL

-

2 48 6

6 ADAS-Cog ADCS-IADL

	(13.3mg/24h) N = 265	(9.5mg/24h) N = 271	(13.3mg/24h) - (9.5mg/24h)
			DLSM 95% CI P

	(13.3mg/24h) N = 265	(9.5mg/24h) N = 271	(13.3mg/24h) - (9.5mg/24h)

-

1.1mg/kg/ 1.6mg /kg/

0.75mg /kg/

AUC 13.3mg/24

/ 0.5-1

/ /

8 C_{max} 10-16

24

40

8

50%

0 1 2

4.6mg/24 17.4mg/24

C_{max} AUC

4.6mg/24

17.4mg/24 9.5mg/24 13.3mg/24 17.4mg/24

4.6mg/24 AUC 2.6 4.9 7.8

(FI) $((C_{max}-C_{min})/C_{avg})$ 0.57-0.77

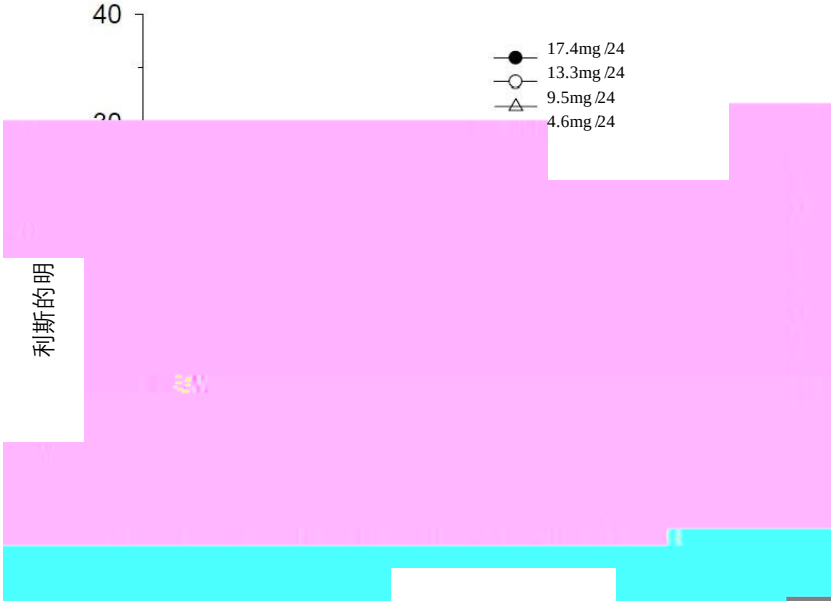
FI=3.96 6mg/ -6.24

12mg/ 17.4mg/24

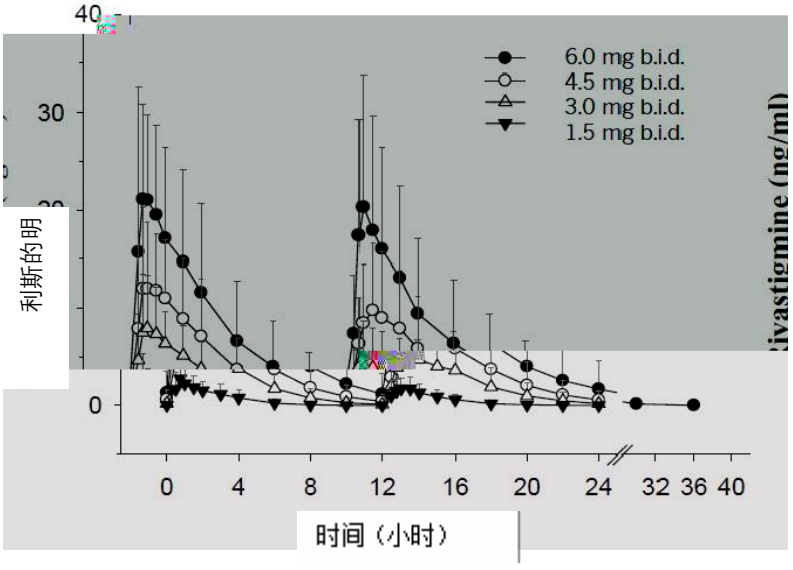
9-10mg 2 / 18-20mg/

9.5mg/24 6mg 2 / 12mg/

1 24



2 2 / /



/

/ kg 43% C_{max} 49% AUC_{0-24h}

74% 103%

45% C_{max} 43% AUC_{0-24h}

71% 73%

NAP-226-90

65kg 35kg 2

100kg

24 67%

NAP266-90 AUC

3 2

20-30%

/ NAP226-90

2 1

/ 40%

1.8-2.7L/kg

/

<10%

CYP1A2,CYP2D6,CYP3A4/5,CYP2E1,CYP2C9,CYP2C8,CYP2C19, CYP2B6

P450 /

- AUC 0.7 3.5

NAP226-90

/

^{14}C- 24 24

>90% 1%

3 2.1 2.8

/

C_{max} 60% AUC 2

3mg 6mg /

n=7, Child-Pugh 5-6 n=3, Child-Pugh 7-9 n=10,

n=10 60-65%

---

7 / 30 /

36

JX20200001

Luye Pharma AG

Am Windfeld 35, 83714 Miesbach, Germany

Luye Pharma AG

Am Windfeld 35, 83714 Miesbach, Germany

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264670

0535-6717618

0535-6717718

www.luye.cn

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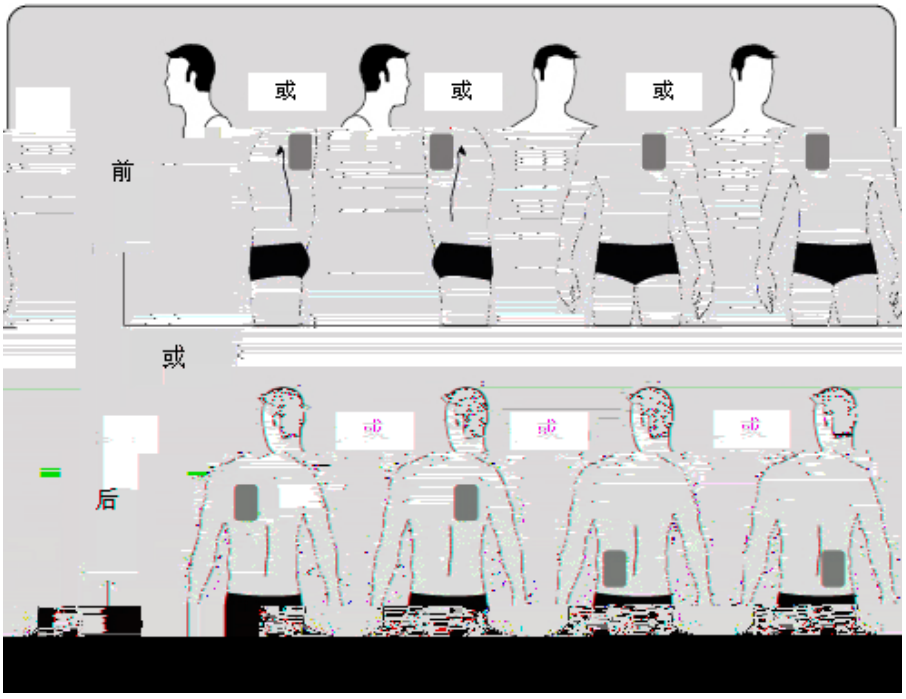
-
  2
- 3
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A

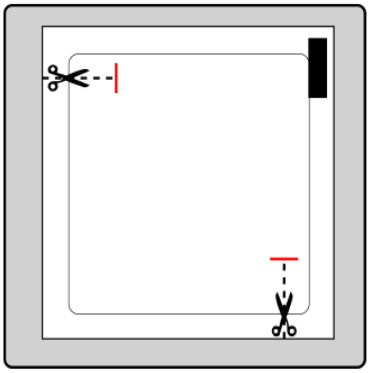


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1. B

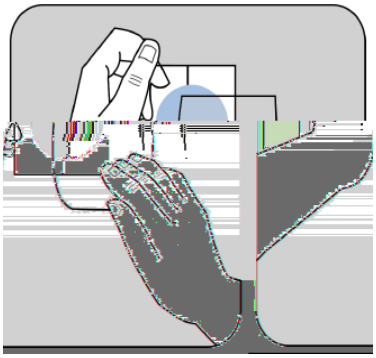
B



2.

C

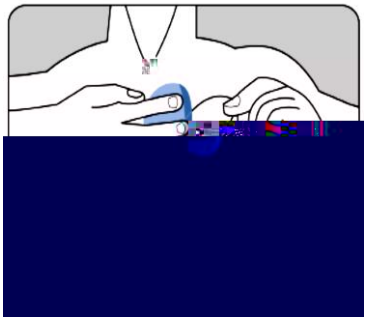
C



3.

4. (D)

D



5. E

E