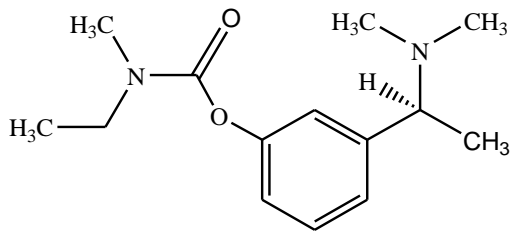




Rivastigmine Transdermal Patch  
Lisidiming Toupitieji

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



C<sub>14</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub>

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 <sup>2</sup>
9.5mg/24	9.5mg/24	13.8mg	9.2cm <sup>2</sup>

---

4.6mg/24

---

4  
9.5mg/24

4.6mg/24

---

9.5mg/24

---

/

3

4.6mg/24

---

/

• / <6mg/ 4.6mg/24

• / 6-12mg/ 9.5mg/24

---

- 50kg

-




\* 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%

	<u>9.5mg/24</u> <u>N=247</u> <u>n (%)</u>	<u>12mg/</u> <u>N=251</u> <u>n (%)</u>
	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

•

\_\_\_\_\_

/

/

\_\_\_\_\_

\_\_\_\_\_

/

\_\_\_\_\_

/

/

/

\_\_\_\_\_

88% 65

55% 75

/

P450

---

---

/

---

/

/

/

---

/

---

---

-

/

-

-

---

n=75

549

12mg/

/

/

23%

---

/  
/  
/

/

/

—

/

/

—

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 24 p	n=248 27.0±10.3 -0.6±6.4 0.005*1	n=253 27.9±9.4 -0.6±6.2 0.003*1	n=281 28.6±9.9 1.0±6.8
ADCS-CGIC p	n=248 3.9±1.20 0.010*2	n=253 3.9±1.25 0.009*2	n=278 4.2±1.26
ADCS-ADL 24 p	n=247 50.1±16.3 -0.1±9.1 0.013*1	n=254 49.3±15.8 -0.5±9.5 0.039*1	n=281 49.2±16.0 -2.3±9.4

ITT  
1

LOCF

ADAS-Cog

ADCS-ADL

2

CMH

van Elteren

ADCS-CGIC

<4

24

5

ADAS-Cog

4

ADCS-CGIC

ADCS-ADL

	%		
	9.5mg/24	12mg/ <sup>®</sup>	
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

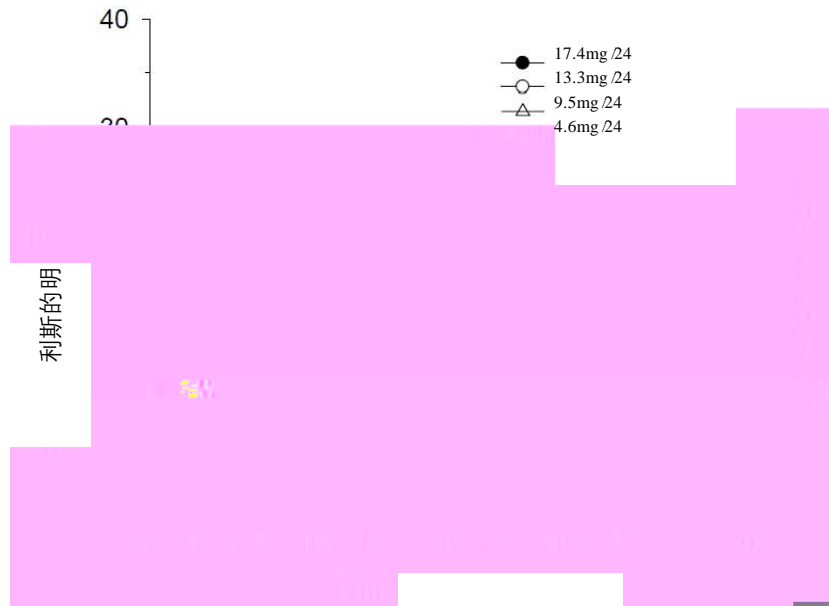
95% CI

P

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

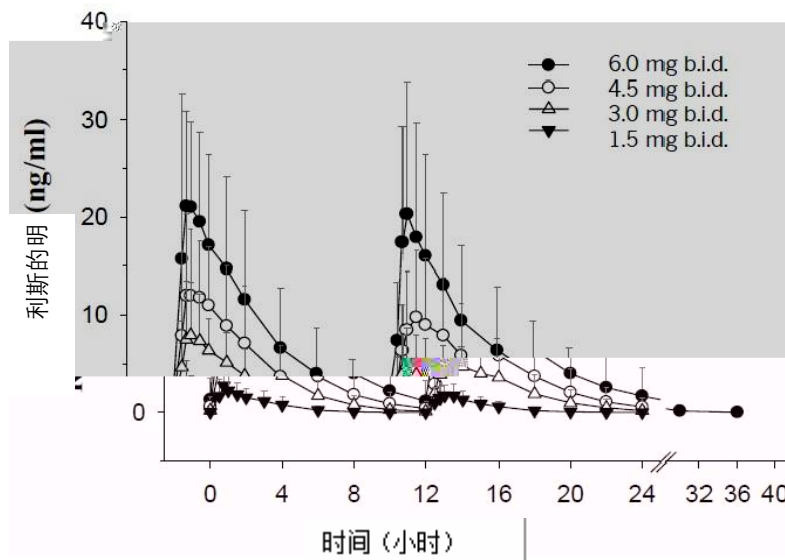
	1.1mg/kg/		1.6mg /kg/	
	0.75mg /kg/			
		AUC		13.3mg/24
—		/		0.5-1
		/	/	
8		C <sub>max</sub>		10-16
	24			
		40		
		50%		8
	0 1 2			
	4.6mg/24	17.4mg/24		
			C <sub>max</sub>	AUC
			4.6mg/24	
17.4mg/24		9.5mg/24	13.3mg/24	17.4mg/24
	4.6mg/24	AUC	2.6 4.9 7.8	
(FI)			((C <sub>max</sub> -C <sub>min</sub> )/C <sub>avg</sub> )	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<sub>max</sub> 49% AUC<sub>0-24h</sub>  
74% 103%

45% C<sub>max</sub> 43% AUC<sub>0-24h</sub>  
71% 73%

	65kg	35kg	NAP-226-90
100kg			2
	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		
— /			
<sup>14</sup> C-	24		24
>90%		1%	
3	2.1	2.8	
—			
—			



15

15

264670

0535-6717618

0535-6717718

[www.luye.cn](http://www.luye.cn)

?

---

•

•

•

1

•

•

•

•

•

•

24

•

14

•

•

•

2

•

3

•

•

1

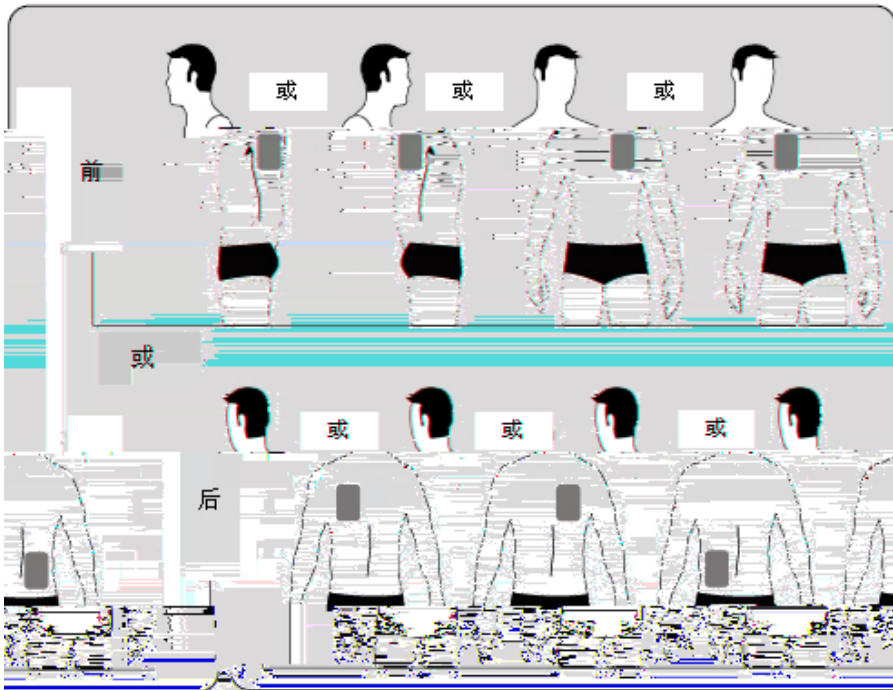
1

?

A

- 
- 
- 
- 

A

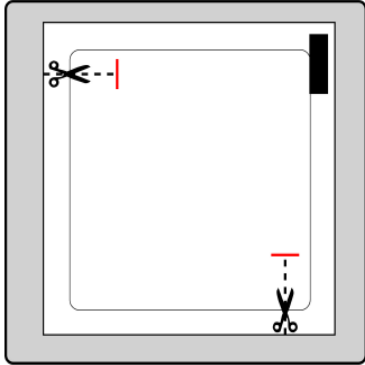


:

1.

B

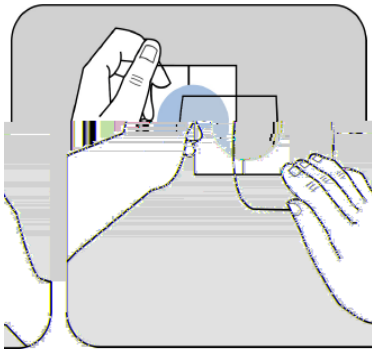
**B**



2.

**C**

**C**

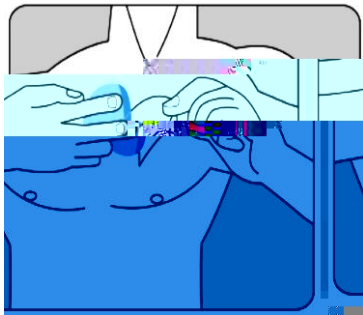


3.

4.

( **D** )

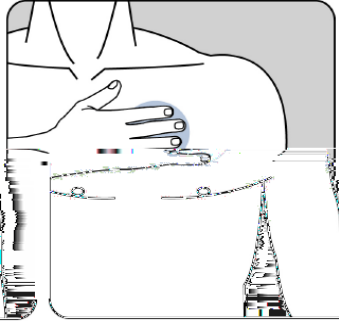
**D**



5.

**E**

**E**



6

---

- 
- 
- 
- 

---