2021 10 26

2021 12 30

合源® 思源清®

/ **ADHD**

ADHD

/

6 18

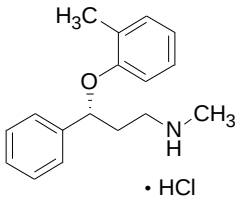
12 **2200** **1 ADHD 1**

0.4% 5/135 **851**

Atomoxetine Hydrochloride Capsules

Yansuan Tuomoxiting Jiaonang

- -N- -3- -3- O-



$C_{17}H_{21}NO \cdot HCl$

291.82

/ ADHD

25mg($C_{17}H_{21}NO$)

70 - 0.5mg/kg

3 1.2mg/kg

1.2mg/kg/

1.4mg/kg 100mg

70 - 40mg

3 80mg

2 4 100mg

70kg 100mg

/

ADHD 6-15

1.2-1.8mg/kg/

120mg 150mg

- HI ADHD HI

Child-Pugh ClassB HI 50% HI

Child-Pugh ClassC 25%

CYP2D6 CYP2D6 Poor metabolizers,PM

_____- CYP2D6 CYP2D6 PM

70 0.5mg/kg/ 4

1.2mg/kg/

CYP2D6 70

40mg/ 4

80mg/

/

ADHD DSM-IV 7 -

2

	2	1
	3	0
	16	4
	3	1
	19	15
c	11	4
	5	2
	2	1

a 2%

2%

b

c

2 **18**

	BID		**QD**	
	N=715	**N=434**	**N=882**	**N=500**
a	17	13	18	7
	11	8	11	4
	7	6	13	4
b	2	1	1	0
	6	4	9	2

[c]	2	0	1	1

[a]

[b] Breslow-Day

[c] Breslow-Day 0.05 P 0.1

2% CYP2D6 PM PM

CYP2D6 EM PM 11%,EM 6% PM 7% EM 4%

PM 7% EM 4% [1] PM 7%,EM EM 4% PM 5% EM

1% PM 4% EM 2% PM 3% EM 1%

PM 3% EM 1% PM 3% EM 1% PM 2% EM

1% PM 2% EM 1% PM 4% EM 2%

[1]

_____- 11.3% 61/541

3.0% 12/405 1

0.9% N=5 0.9% N=5 0.6% N=3 0.6% N=3 0.4%

N=2 0.4% N=2 0.4% N=2 0.4% N=2 0.4%

N=2 0.4% N=2

_____-

0.1% 1/748

0/43 0.1% 1/705

_____- 3 2%

5% 2

ō

	3	1
	20	5
	26	6
	8	3
b	7	4
	4	2
	4	2
	10	6
	3	0
	2	1
	5	3
	2	1

f	8	1
g	3	2
f / f	4	1
	4	1
	3	0

a 2%

2%

b

c

d

e

f STRATTERA N=943 N=869

g STRATTERA N=754 N=691

2% CYP2D6 PM PM CYP2D6 EM PM 4% EM 1% PM 35% EM 17% PM 11% EM 7% PM 5%, EM 2% PM 23% EM 15% PM 5% EM 1% PM 19%, EM 11% PM 7%, EM 3% PM 5% EM 3% PM 3% EM 1% PM 6%, EM 1% PM 21%, EM 9% PM 6%, EM 2% PM 15% EM 7% PM 3% EM 1%

-

4 2%

_____-QT

_____-

_____-

_____-

_____-

_____-

_____-

ADHD

_____-

_____-

MAOI

MAOI MAOI MAOI

MAOI

15-20mmHg 20 /

/ ADHD

6 18

12 ADHD 11 1 2200

1357 851

0.4% 5/1357

2200 1

12

ADHD MDD

6000

1

“ ”

120 [20 × ULN]

2 × ULN 40

12

: “ ”

-

- ADHD

:

≥15mmHg ≥20mmHg ≥20bpm[a]

	b				b			
	%	%	%	%	%	%	%	%
DBP ≥15mmHg	21.5	14.1	9.3	4.8	12.6	8.7	4.8	3.5
SBP ≥20mmHg	12.5	8.7	4.9	3.3	12.4	7.8	4.2	3.2
HR ≥20bpm	23.4	11.5	12.2	3.8	22.4	8.3	10.2	2.0

[a] :bpm= / :DBP= HR= mmHg= SBP=

[b]

0% 0/934

0.3% 5/1597 EM 5.0 / PM

9.4 /

EM/PM PM EM 11

/ 7.5 / PM

0.5% 2/402

1.5% 8/540

EM/PM PM

EM 4.21 2.13mmHg , EM PM:2.75

EM:2.40mmHg PM

0.2% 12/5596 0.8% 46/5596

1.8% 6/340

0.5% 1/207

0.2% 1939

4 1056

ADHD

:

ADHD ADHD

21/1308 1.6%

9/806 1.1%

1.33[95% 0.67-2.64-] 6/1697 0.35%

4/1560 0.26%

1.38[95% 0.39-4.88-]

ADHD 1.7% 9/540 5.6%

30/540 0% 0/402 0.5% 2/402 2

4

9-12

3 17.9

0.5 12

3 19.4 0.4 1

1: 3

AUC 10 5 7% PM CYP2D6

PM PM CYP2D6 PM

0.8mg/kg/ , 1.2mg/kg/ 1.30mg/kg/

± 0.29mg/kg/ PARS

158 26 16%

16 18-65 442

ADHD DSM-IV 23% 2

40mg/ 100mg/ 83mg/ ± 19.5mg/

LSAS

413 149 36.1%

_____-

_____-

“ ”

_____-

_____-

4

_____-

_____-

____-

____- 24 24

_____-

____

2-4% 15-20%

____

6

MAOI

CYP2D6

EM CYP2D6

PM

EM AUC 6 8 C_{ss} C_{max} 3 4

PM P450

β_2

600mcg 2 60mg 5

21

200-800mcg 80mg.

5

P450

P450 CYP1A2 CYP3A CYP2D6

CYP2C9

CYP3A - 60mg 12

CYP3A4 5mg AUC 15%

CYP3A

CYP2D6 - 40 60mg 13

CYP2D6 50mg

CYP2D6

,

pH

pH /

1400mg

QT

_____- 6 18 4

ADHD DSM-IV

/

ADHD ADHD Rating Scale-IV-Parent Version ADHDRS

/

intent-to-treat ADHDRS

DSM-IV ADHD

1 8 18 N=297 8

0.5 1.2 1.8mg/kg/

ADHDRS ADHD

1.8mg/kg/ 1.2mg/kg/

0.5mg/kg/

2 6 16 N=171 6

1.5mg/kg/ 1.3mg/kg/ ADHDRS

ADHD

2 7 13 3 N=147 4 N=144 9

2.0mg/kg/ 1.6mg/kg/ ADHDRS

ADHD

12 12 17

- 6-15 ADHD

1.2-1.8mg/kg/ 10 4 DSM-IV ADHD

N=292 N=124

CGI-ADHD-S ≤2 ADHDRS-IV-Parent

25% 8

N=81 N=82 CGI-ADHD-S

2 ADHDRS-IV-Parent 90%

2 DSM-IV ADHD 18

ADHD

30 CAARS ADHD

18 ADHD CAARS /

intent-to-treat

2 10 5 N=280 6 N=256

60

120mg/ 95mg/

CAARS ADHD

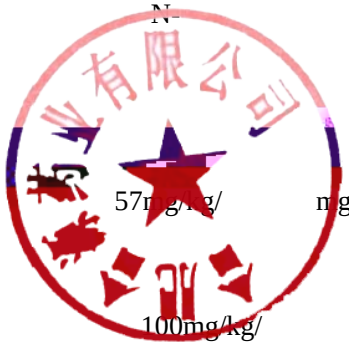
<42 ≥42

/ ADHD

Ames CHO

DNA UDS CHO

N- Ames UDS



57mg/kg/ mg/m^2 6

100mg/kg/ 3 1

30mg/kg/ mg/m^2 100mg/kg

23 AUC AUC 3.3

0.4

50mg/kg/ mg/m^2 6

2 10 2 1

25mg/kg 13mg/kg

2 10 40mg/kg/

mg/m^2 5

20mg/kg/

150mg/kg/ mg/m^2

17

2 47 458mg/kg/

8 5 mg/m^2

AUC AUC 1.8 0.2

39 26 mg/m^2

10

1 10 50mg/kg/ mg/m^2 0.2 2

8 10 50mg/kg

10 50mg/kg 50mg/kg 50mg/kg

15 10 50mg/kg 50mg/kg 30 50mg/kg

60

P450 2D6

CYP2D6 5 CYP2D6

PM 7% 2% CYP2D6 PM

1% [EM] 10

AUC 5 24 CYP2D6

400

mg/kg

Cmax AUC

_____- EM PM 63% 94%

1-2 Cmax

AUC Cmax 37% Tmax 3

Cmax 9%

0.85L/kg

98%

_____- CYP2D6 EM

PM EM PM

AUC 10 Css Cmax 5 CYP2D6 PM

CYP2D6

CYP2D6

CYP2D6 4-

4-

EM 1% PM 0.1% 4- CYP2D6

PM 4- P450 N-

CYP2C19 P450

EM 5% PM 45%

EM 0.35L/hr/kg 5.2

PM 0.03L/hr/kg 21.6 EM

PM AUC 10 Css Cmax 5 EM 4-

N- 6 8 PM N-

34 40

4- -*O*- 80%

17%

3%

/ 7 / 1 / 14 / 1 / 14 / 2 /

24

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