2008 09 28

2009 03 13

2010 05 31

2011 11 28

2011 12 08

2012 06 07

2013 03 14

2013 05 22

2013 12 05

2014 05 18

2015 12 24

2016 11 01

2017 02 24

2017 08 28

2017 09 25

2018 03 13

2018 10 10

2019 05 29

2019 06 27

2020 06 22

2020 06 28

警示语

会增高痴呆相关性精神病老年患者的死亡率

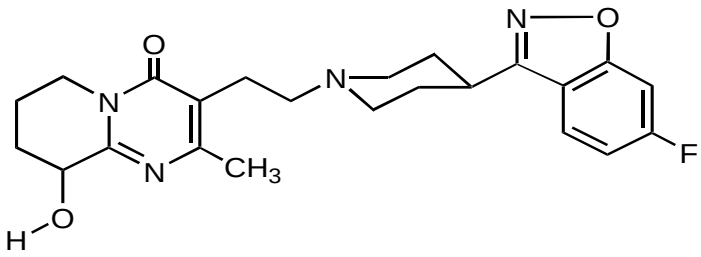
与安慰剂相比，使用非典型性抗精神病药物治疗患有痴呆相关性精神病的老年患者时，死亡的风险会增加。对在患有痴呆相关精神病的老年患者中进行的17项安慰剂对照临床试验（平均众数治疗时间为10周）的分析显示，药物治疗组患者死亡的危险性为安慰剂对照组的1.6 - 1.7倍。在一项典型的10周对照试验中，药物治疗组的死亡率为4.5%，安慰剂对照组为2.6%。虽然死亡原因各异，但大多数死于心血管病（如心衰、猝死）或感染（如肺炎）。本品未被批准用于治疗痴呆相关性精神病患者(参见【注意事项】）。

®

Paliperidone Extended-Release Tablets

Palipaitong Huanshi Pian

± -3-[2-[4-(6- -1,2- -3-)-1-]]-6,7,8,9- -9- -2- -4H- [1,2-*a*] -4-



$C_{23}H_{27}FN_4O_3$

426.49

200K K29-32

200K K29-32

7000K K29-32

3350

398-10 3350

HPMC 2910 6 cP HPMC 2910 15 cP

400

HPMC 2910 6 cP

3 mg/ 6 mg/

9 mg/

12-17 ≥29Kg

3 mg 6 mg 9 mg

6 mg

6 mg

12 mg/

3 mg/

6 mg/ 5

3 mg/ 12 mg/

6

12-17

12-17 ≥29Kg 3 mg

3 mg/ 5

51 kg 6 mg 51 kg

12 mg

51Kg> ≥29Kg	3mg/	3-6mg/	6mg/
≥51Kg	3mg/	3-12mg/	12mg/

50 mL/min <80 mL/min 3 mg

6 mg 10 mL/min

<50 mL/min 3 mg 3 mg

<10 mL/min

Child-Pugh A B

10 mL/min <50 mL/min 3 mg

3 mg <10 mL/min

<12

-
-
-
- QT
-
-
-
-
-

-
-
-
-
-
- TTP
-
-
-
-

5%

2%

6 1205

850 3 mg~12 mg

3 mg~15 mg n=104

MedDRA

ADRs /

QT

1 6 ≥2%

1 6 2%

	3 mg 1	**6mg 1**	**9 mg 1**	**12 mg 1**	
/	**N=127** %	**N=235** %	**N=246** %	**N=242** %	**N=355** %
	11	12	14	14	12
	6	5	4	5	4
	5	2	7	7	2
	5	3	7	5	3
	4	3	8	10	4
	3	3	4	3	3
	2	1	4	3	1
	1	1	4	4	1
	1	5	3	6	4
	0	<1	2	1	0
	0	0	2	0	0
	9	4	4	7	4
	2	7	7	7	3
	3	1	3	<1	2
	2	1	1	<1	0
	2	0	2	1	1
	2	1	2	4	1
	2	3	4	5	5
	2	3	1	3	1
	1	3	2	2	1
	0	<1	1	4	<1
	2	<1	2	2	1
	2	1	2	2	1

12 12 2

12 12 N = 545 ADRs

/

≥1/10

≥1/100 <1/10

2 ≥2% 12-17

2 **2%**

	1.5 mg 1	**3 mg 1**	**6 mg 1**	**12 mg 1**	
/	**N=54**	**N=16**	**N=45**	**N=35**	**N=51**
	4	0	4	0	2
	9	6	7	14	22
	0	0	2	9	4
	6	13	13	26	2
	4	6	11	17	0
	9	6	4	14	4
	2	6	7	11	0
	2	0	4	9	0
	0	0	0	11	0
	2	6	2	3	0
	2	6	2	3	0
	4	0	2	0	2
	0	0	4	0	0
	0	6	0	0	0
	0	0	0	3	0
	0	0	0	3	0
	0	0	0	3	0
	0	0	4	3	0
	0	0	0	3	0
	0	6	7	6	0
	0	0	2	0	0
	0	0	2	0	0
	0	6	11	3	10
	0	0	2	9	12
	2	6	2	0	0

	2	0	2	0	2
	0	0	0	3	2
	0	0	0	3	0
	0	0	2	3	0
	0	0	0	3	0
	0	0	2	0	0
	0	0	4	0	0
	0	6	0	0	0
	0	0	0	3	0
	4	0	2	3	0
	0	0	2	3	0
	7	6	2	3	0

6

3% 1%

2% 0%

6

<1%

6 2%

12 mg 9 mg

6

2%

6

EPS

-

/

6 EPS

EPS 1 Simpson-Angus

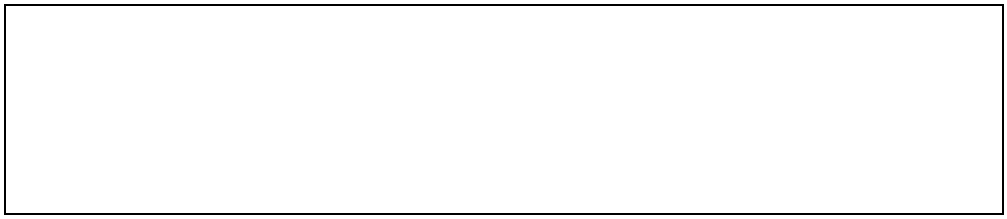
2 Barnes

3 EPS 3 4 EPS 4

Simpson-Angus EPS 9 mg 12 mg

EPS 3 mg 6 mg

qÎ 2 qÍ ¯+X Ç6ö.á7-9Ÿ(™"ë+Ç3W U



EPS

5

5 MedDRA EPS ——

		1.5 mg	**3 mg**	**6 mg**	**12 mg**
EPS	**N=51)**	**N=54**	**N=16**	**N=45**	**N=35**
EPS AE	0	6	25	22	40
	0	4	6	11	17
	0	2	0	11	14
	0	2	6	7	11
	0	0	6	2	14
	0	2	6	2	6

6

C HDL LDL

6 ≥ 7%

3 mg 6 mg 7% 6% 5% 9 mg

12 mg 9% 9%

/

6a 9 8 1

/

≥2%

6a 9 8 1

/

/
* * * *
*

6b 9 8 1

/

<2%

6b 9 8 1

/

<2%

/

* *

QT

γ-

*

*

*

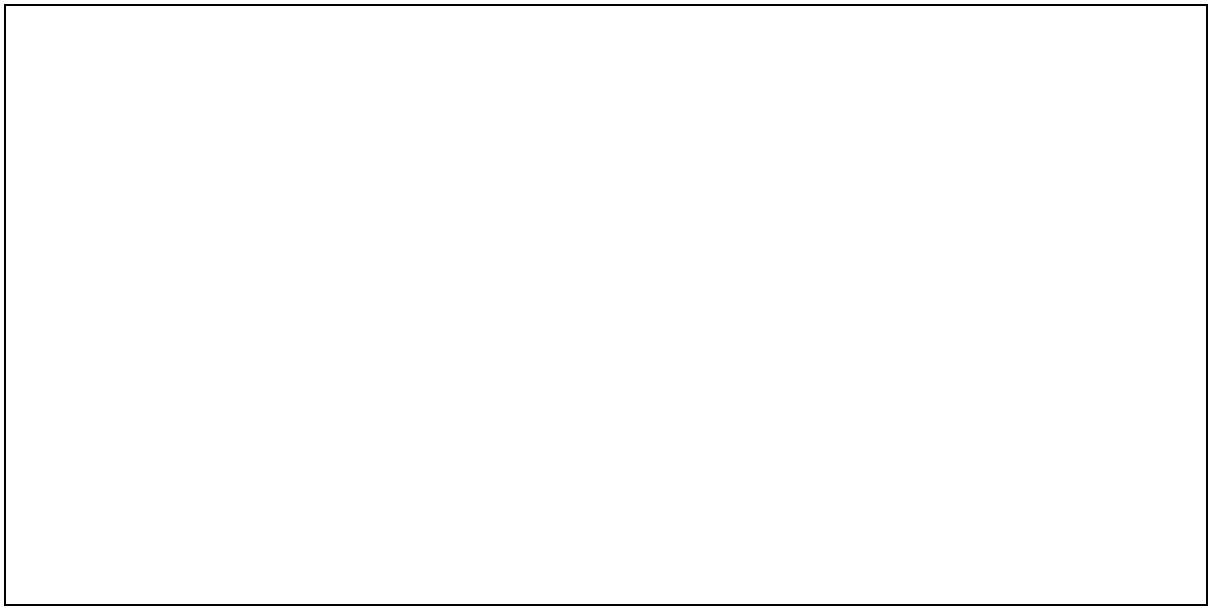
6c / 9

8 1

6c **/** **9**

8 **1**

/



14

6

14

7

≥10%

1% 10%

0.1% 1%

0.01% 0.1%

<0.01%

7 8

7

Stevens-Johnson /

8 /

*

Stevens-Johnson /

*	0.05%
0%	0.14%

NMS NMS

EPS

NMS 1 2

3

NMS

NMS

NMS

QT

QT QTc

QTc 1A III

QTc QT

QTc /

1 2 3 QTc

4 QT

400 mg QT QT

6

QT n = 141 8 mg n=50 8 1.5

QTcLD 12.3msec 90%CI:8.9;15.6 8 mg

12 mg

C_{max} ss 113 ng/mL 45 ng/mL 4 mg

C_{max} ss = 35 ng/mL 2 1.5 QTcLD

6.8msec 90% CI: 3.6; 10.1 60 ms

QTcLD 500 ms

ECG 12

mg 6 60 ms 62 ms

QTcLD 500 ms

12-17 6 9a

9a **12-17** **6**

			1.5 mg/	3 mg/	6 mg/	12 mg/
					mg/dL	
		N=41	N=44	N=11	N=28	N=32
		0.8	-1.4	-1.8	-0.1	5.2
		3%	0%	0%	0%	11%
<100 mg/dL	≥126 mg/dL	1/32	0/34	0/9	0/20	3/27

12-17 6 9b

9b **12-17** **6**

		1.5 mg/	3 mg/	6 mg/	12 mg/
				mg/dL	
	n=39	**n=45**	**n=11**	**n=28**	**n=32**
	-7.8	-3.3	12.7	3.0	-1.5
LDL	**n=37**	**n=40**	**n=9**	**n=27**	**n=31**
	-4.1	-3.1	7.2	2.4	0.6
HDL	**n=37**	**n=41**	**n=9**		

6 182

12-17

6 ≥7% 10

10 **12-17** **6**

		1.5 mg/	**3 mg/**	**6 mg/**	**12 mg/**
	n=51	**n=54**	**n=16**	**n=45**	**n=34**
kg					
	0.0	0.3	0.8	1.2	1.5
	2%	6%	19%	7%	18%

≥7%

33%

182

0.1 4%

D_2

GnRH

“ ” Meckel

α

6 3 mg, 6 mg, 9 mg, 12 mg

0.8% 7/850 0.3% 1/355

<1/10,000

/

$<1\times10^{9}$/L

VTE

VTE VTE

6

3 mg, 6 mg, 9 mg, 12 mg 0.22%

0.25%

65

α

TTP

TTP

TTP

α1a

α1a α1

/

Claims

=1.26 95% CI 1.02-1.56

20-34

/

9- 9-

9-

<12

114 ≥65 21 ≥75 6

3 mg~12 mg ≥65 6

3 mg~15 mg

n = 1796

125 7.0% ≥65 22 1.2% ≥75

CYP450

CYP450 CYP1A2 CYP2A6 CYP2C8/9/10 CYP2D6 CYP2E1 CYP3A4 CYP3A5

P- P-

12mg 500mg 2000mg

CYP1A2 CYP2A6 CYP2C9 CYP2C19

CYP2D6 CYP3A4

P-gp

CYP2D6

3 mg 20 mg/ CYP2D6

CYP2D6 16% 90% CI: 4, 30

200 mg C_{max}
AUC 37% P-gp
35%
CYP

12 mg 2 500 mg/
C_{max} AUC 50%

405 mg

QT

QT α

/

β α

DSM-IV 37

6 3 mg-15 mg

3 mg/ 6 mg/

9 mg/ 12 mg/ 15 mg/

PANSS PANSS

/ /

PSP PSP

3 n = 1665 PANSS

PSP

65

DSM-IV PANSS ≤ 70

PANSS ≤4 8

6 3-15mg 1

PANSS PANSS

6

1.5-12 mg/ N = 149

N = 51 12-17 DSM- PANSS

3 mg 6 mg 12 mg

11 **R076477-PSZ-3001** **6**

LOCF

	N=51	1.5 mg N=54	3 6 mg* N=48	6 12 mg** N=47
PANSS (SD) (SD) P- (vs) (SE)	90.6 (12.13) -7.9 (20.15)	91.6 (12.54) -9.8 (16.31) 0.508 -2.1 (3.17)	90.6 (14.01) -17.3 (14.33) 0.006 -10.1 (3.27)	91.5 (13.86) -13.8 (15.74) 0.086 -6.6 (3.29)
n (%) n (%) P (vs)	17 (33.3) 34 (66.7)	21 (38.9) 33 (61.1) 0.479	31 (64.6) 17 (35.4) 0.001	24 (51.1) 23 (48.9) 0.043

PANSS ≥20%

LOCF =

* < 51 kg 3 mg ≥ 51 kg 6 mg

** < 51 kg 6 mg ≥ 51 kg 12 mg

8 18

≥12 N = 112 N = 114 3 mg/

9 mg/ 8 26 PANSS

26 PANSS ≥20%

12 **R076477-PSZ-3003** **26**

LOCF

	3-9 mg N=112	5-15 mg N=114
PANSS **8** (SD) (SD) P- (vs) (SE)	89.6 (12.22) -19.3 (13.80) 0.935 0.1 (1.83)	92.0 (12.09) -19.8 (14.56)

PANSS **26** (SD) (SD) P- (vs) (SE)	89.6 (12.22) -25.6 (16.88) 0.877 -0.3 (2.20)	92.0 (12.09) -26.8 (18.82)
26 n (%) n (%) P- (vs)	86 (76.8) 26 (23.2) 0.444	93 (81.6) 21 (18.4)

PANSS ≥ 20%

LOCF =

2 D_2 5- 2 $5HT_{2A}$

1 2 H_1

1 2

+ - - -

Ames

2.5 mg/kg/

0.63 mg/kg mg/m^2

2.5 mg/kg/

Beagle

0.31~5.0 mg/kg

10 mg/kg/ 5 mg/kg/

mg/m^2 8

mg/m^2

Swiss albino Wistar

0.63 2.5 10 mg/kg 18

25

mg/m^2

D_2

24 73

0.63 mg/kg/ AUC

2.5 mg/kg/

2~3

40 0.31

1.25 5 mg/kg/ 0.31 mg/kg/ +

AUC

12

24

C_{max} 3mg-12 mg

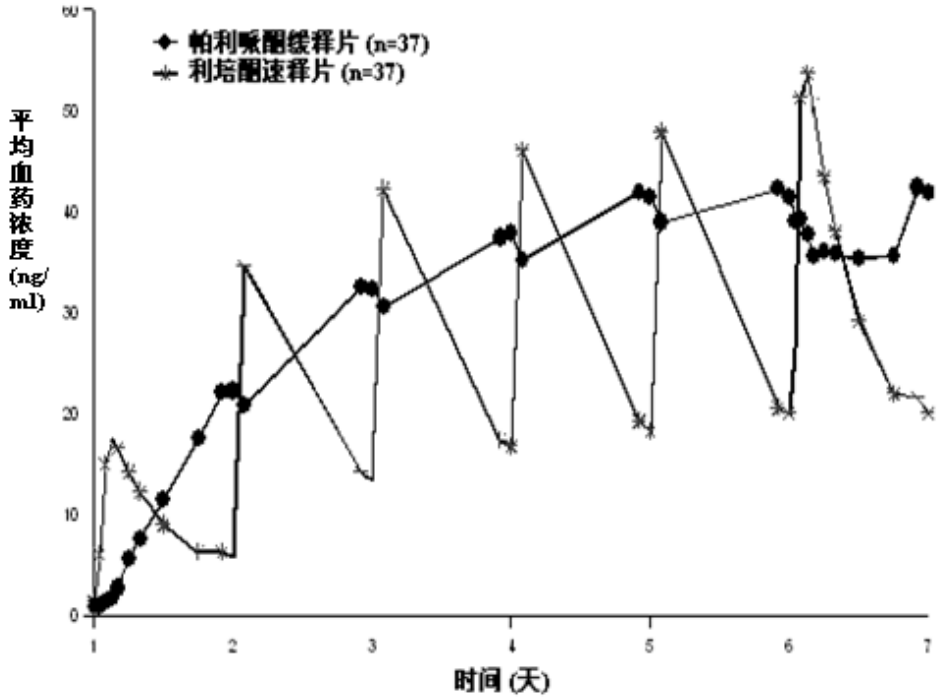
23

4-5 9 mg

1.7 1.2-3.1

12mg 1 4mg

38% 125% 1



1 12mg 2mg 6 / 1 6

1 2mg 2-6 4mg/ +

, + - AUC +

- 1.6

28%

/ 12 mg

C_{max} AUC 60% 54%

487 L

74%

CYP2D6 CYP3A4

5 1 mg ^{14}C 59%

51%-67% 32% 26%-41% 6%-12%

80% 11% 4

10%

CYP2D6

3 mg

CrCl = 50 mL/min < 80 mL/min

32% CrCl = 30 mL/min < 50 mL/min 64%

CrCl = 10 mL/min < 30 mL/min 71% AUC_{inf}

1.5 2.6 4.8 24

, 40 51 23 CrCl ≥ 80 mL/min

Child-Pugh B

12-17 *≥29Kg*

<51 kg <112 lbs

≥51 kg ≥112 lbs 23%

CYP1A2

15-30

/ /

7 / 28 /

24

JX20100237

3mg: H20160549

6mg: H20160550

9mg: H20160551

3mg: J20170010

6mg: J20170011

9mg: J20170012

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