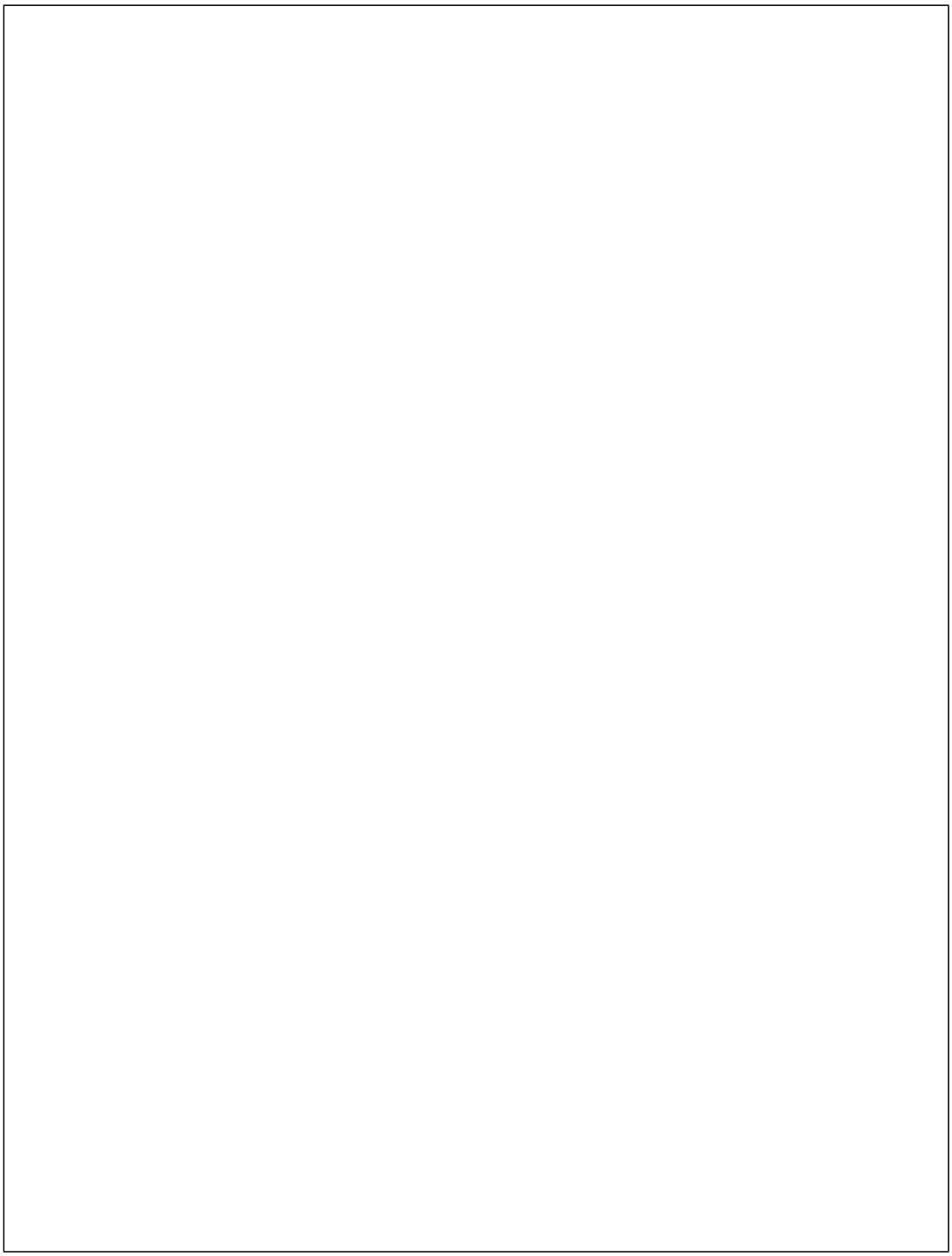
○

2021 03 30

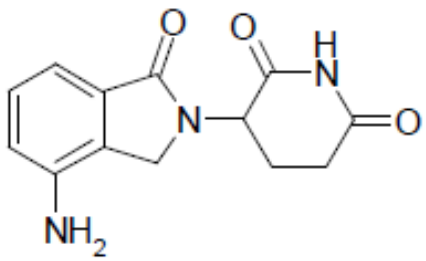
2021 06 17



Lenalidomide Capsules

Lainadu’an Jiaonang

3- 4- -1- -1,3- -2*H* - -2- -2,6-



$C_{13}H_{13}N_3O_3$

259.26

5mg 10mg

ANC <1.0 ×10^9/L / <50 ×10^9/L

25mg 28 1 21

25 mg 28 1

8 15 22 40 mg

1

28 1 8 15 22 40 mg/	28 1 8 15 22 20 mg/

12 12

2

3 4

3 4

-

	a	a
	25 mg	40 mg
-1	20 mg	20 mg
-2	15 mg	12 mg
-3	10 mg	8 mg
-4	5 mg	4 mg
-5	5 mg	NA

a

-

< 25×10^9/L b

<25 × 10^9/L

5mg

- ANC

< 0.5 × 10^9/L
ANC < 1 × 10^9/L
15
7
15
28

G-CSF

<0.5 × 10^9/L

5mg
G-CSF

-
- ANC 1,000/μL μL

3/4

7

15 28

<60 mL/min

mL/min	28 1 21 25 mg/
mL/min < 60 mL/min	28 1 21 10 mg / [e]
< 30 mL/min	28 1 3 5 7 9 11 13 15 17 19 21 15 mg/ 3
< 30 mL/min	28 1 21 5 mg/

[d] Cockcroft-Gault

[e] 10mg 2
10mg 15mg 3

<30mL/min 28
1 21 15mg 3/4

	1 21 15 mg
-1	1 21 10mg
-2	1 21 5 mg

1

2

L

L 2

4 2 3

Rd 6 0.7%

9.6%

4 Rd Rd 18 MPT

≥ ≥

%	173 (32.5)	177 (32.8)	154 (28.5)	39 (7.3)	46 (8.5)	31 (5.7)
	150 (28.2)	123 (22.8)	124 (22.9)	41 (7.7)	33 (6.1)	32 (5.9)
c	114 (21.4)	102 (18.9)	76 (14.0)	13 (2.4)	7 (1.3)	7 (1.3)
f	29 (5.5)	31 (5.7)	18 (3.3)	<1%	< 1%	< 1%
	242 (45.5)	208 (38.5)	89 (16.5)	21 (3.9)	18 (3.3)	8 (1.5)
%, f	109 (20.5)	78 (14.4)	60 (11.1)	7 (1.3)	9 (1.7)	< 1%
f	57 (10.7)	28 (5.2)	36 (6.7)	<1%	< 1%	0 (0.0)
c	170 (32)	145 (26.9)	116 (21.4)	37 (7)	34 (6.3)	28 (5.2)
f	109 (20.5)	102 (18.9)	61 (11.3)	< 1%	< 1%	< 1%
f	101 (19.0)	71 (13.1)	66 (12.2)	9 (1.7)	8 (1.5)	8 (1.5)
f	87 (16.4)	77 (14.3)	62 (11.5)	16 (3.0)	15 (2.8)	14 (2.6)
f	79 (14.8)	66 (12.2)	61 (11.3)	8 (1.5)	8 (1.5)	7 (1.3)
f	67 (12.6)	59 (10.9)	36 (6.7)	< 1%	< 1%	< 1%
f	60 (11.3)	51 (9.4)	39 (7.2)	6 (1.1)	< 1%	< 1%
f	43 (8.1)	35 (6.5)	29 (5.4)	< 1%	8 (1.5)	< 1%
f	40 (7.5)	19 (3.5)	10 (1.8)	< 1%	< 1%	< 1%
c	90 (16.9)	59 (10.9)	43 (7.9)	9 (1.7)	6 (1.1)	3 (0.6)
f	80 (15)	54 (10)	33 (6.1)	0 (0.0)	0 (0.0)	0 (0.0)
f	76 (14.3)	63 (11.7)	41 (7.6)	8 (1.5)	8 (1.5)	< 1%
c,%, f	69 (13.0)	53 (9.8)	31 (5.7)	< 1%	8 (1.5)	< 1%
c, @	93 (17.5)	87 (16.1)	56 (10.4)	60 (11.3)	57 (10.5)	41 (7.6)
%	35 (6.6)	25 (4.6)	21 (3.9)	7 (1.3)	4 (0.7)	1 (0.2)
f	33 (6.2)	23 (4.3)	15 (2.8)	< 1%	< 1%	0 (0.0)
f	32 (6.0)	17 (3.1)	13 (2.4)	0 (0.0)	< 1%	< 1%
	29 (5.5)	14 (2.6)	16 (3.0)	10 (1.9)	3 (0.6)	3 (0.6)
f	29 (5.5)	24 (4.4)	14 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)
c	< 5%	< 5%	< 5%	8 (1.5)	3 (0.6)	2 (0.4)
c,@	33 (6.2)	26 (4.8)	18 (3.3)	26 (4.9)	20 (3.7)	13 (2.4)
f	75 (14.1)	52 (9.6)	56 (10.4)	< 1%	< 1%	< 1%
f	39 (7.3)	45 (8.3)	22 (4.1)	< 1%	0 (0.0)	< 1%
	233 (43.8)	193 (35.7)	229 (42.3)	97 (18.2)	85 (15.7)	102 (18.9)
	186 (35.0)	178 (33)	328 (60.6)	148 (27.8)	143 (26.5)	243 (44.9)

	104 (19.5)	100 (18.5)	135 (25.0)	44 (8.3)	43 (8.0)	60 (11.1)
	7 (1.3)	17 (3.1)	15 (2.8)	6 (1.1)	16 (3.0)	14 (2.6)
	5 (0.9)	6 (1.1)	7 (1.3)	1 (0.2)	3 (0.6)	5 (0.9)
[f]	121 (22.7)	94 (17.4)	68 (12.6)	< 1%	< 1%	< 1%
[c,e]	117 (22.0)	89 (16.5)	113 (20.9)	30 (5.6)	22 (4.1)	18 (3.3)
[f]	32 (6.0)	31 (5.7)	17 (3.1)	< 1%	< 1%	0 (0.0)
[f]	30 (5.6)	22 (4.1)	14 (2.6)	0 (0.0)		

/

[a] Rd Rd 18 5.0% Rd Rd 18 MPT 2.0%

[b] Rd Rd 18 1.0% Rd Rd 18 MPT 1.0% 3 /4

[c] Rd Rd 18 1.0% Rd Rd 18 MPT 1.0%

[d] Rd /Rd 18

[e] “a”

[f] “b”

@-

%-

*

2 III MM-009 MM-010

28 1 21 25mg

4 28 1 4 9 12

17 20 40mg 28

1 4 40mg

/ 353

/ 350 703 /

44.0 / 23.1

/

39.7% / 70.4%

/ 325 92%

/ 288 82%

-
- 4

43.9% 42.2%

40.5% 38.5% 33.4% 31.4%

21.5% 21.2%

/ 269 76%

/

199 57%

/ 50%

/ 21%

/ 3/4

/

5 6 7 / /

≥ ≥

%	149 42.2	22 6.3
@	111 31.4	83 23.7
@	76 21.5	37 10.6
	28 7.9	4 1.1
	19 5.4	5 1.4
	155 43.9	146 41.7
	97 27.5	82 23.4
	93 26.3	74 21.1

	29 8.2	20 5.7
	24 6.8	8 2.3
	143 40.5	74 21.1
@	136 38.5	96 27.4
@	92 26.1	75 21.4
@	43 12.2	33 9.4
@	35 9.9	22 6.3
	25 7.1	13 3.7
	118 33.4	74 21.1
	91 25.8	65 18.6
	48 13.6	39 11.1
	42 11.9	32 9.1
	82 23.2	59 16.9
	75 21.2	26 7.4
	54 15.3	34 9.7
	36 10.2	25 7.1
	23 6.5	13 3.7

s ' R Ď . ħ

	69 19.5	52 14.9
	61 17.3	40 11.4
%	33 9.3	15 4.3
	28 7.9	20 5.7
	25 7.1	15 4.3

≥ ≥

%	118 33.4	12 3.4
@	43 12.2	22 6.3
@	35 9.9	20 5.7
	14 4.0	1 0.3
	10 2.8	4 1.1
%	8 2.3	0 0.0
	23 6.5	17 4.9
%	29 8.2	12 3.4
@	30 8.5	19 5.4
	5 1.4	1 0.3
	17 4.8	5 1.4
	13 3.7	6 1.7
	9 2.5	0 0.0
@	14 4.0	3 0.9
@	4 1.1	0 0.0
	20 5.7	10 2.9
@	11 3.1	4 1.1
	7 2.0	1 0.3
@	6 1.7	2 0.6
@	13 3.7	4 1.1
	6 1.7	1 0.3

@	5 1.4	1 0.3
	10 2.8	3 0.9
	7 2.0	3 0.9

6

II

MM-021 28 1 21

25mg 28 1 8 15

22

8 9 10 MM-021

199 69 34.7%

69 29 14.6%

3/4

-
-

121/199 60.8% 82/199

41.2% 71/199 35.7%

66/199 33.2%

≥

	121 (60.8)
	71 (35.7)
	43 (21.6)
	35 (17.6)
	82 (41.2)
	66 (33.2)
	43 (21.6)

	25 (12.6)
	13 (6.5)
	13(6.5)
	10 5.0
	24 (12.1)
	17 (8.5)
	13 (6.5)
	11 (5.5)
	10 5.0
	14 (7.0)
	15 (7.5)
	12 (6.0)

AE=

a

b

3 /4 52/199 26.1%

50/199 25.1% 29/199 14.6% 26/199

13.1% 19/199 9.5% 17/199

8.5%

≥

	41 20.6	11 5.5	52 26.1
	42 21.1	8 4.0	50 25.1
	15 7.5	14 7.0	29 14.6
	16 8.0	3 1.5	19 9.5
	13 6.5	1 0.5	14 7.0
	1 0.5	7 3.5	8 4.0
	5 2.5	0 0.0	5 2.5
C	3 1.5	2 1.0	5 2.5
C	1 0.5	3 1.5	4 2.0

	4 2.0	0 0.0	4 2.0
	25 12.6	1 0.5	26 13.1
	8 4.0	0 0.0	8 4.0

	7 3.5
	4 2.0
	2 1.0
	1 0.5
	6 3.0
	2 1.0
	1 0.5
	1 0.5
	2 1.0
	1 0.5
	1 0.5
	1 0.5
	1 0.5
	3 1.5
	2 1.0
	1 0.5
	1 0.5
	1 0.5
	1 0.5
	1 0.5
	1 0.5
	1 0.5
	1 0.5
	1 0.5
	1 0.5
	4 2.0
	1 0.5
	1 0.5
	1 0.5
	2 1.0
	1 0.5
	1 0.5
	1 0.5

	1 0.5

SAE=

[a] 1

[b]

VTE [DVT PE]

ATE

MM-009 MM-010

/ DVT 7.4%

8.2% / 3.1% 3.4%

MM-020 Rd Rd 18 MPT DVT

10.3% 7.2% 4.1% DVT 3.6% 2.0% 1.7%

3 /4 DVT 5.6% 3.7% 2.8% Rd Rd 18 DVT

1% Rd Rd 18 DVT

2.3% 1.5%

MM-009 MM-010

/ 3.7% 3/4 4.0%

/ 0.9% 3/4

MM-020 Rd Rd 18 MPT PE

3.9% 3.3% 4.3% PE 3.8% 2.8% 3.7% PE

3 /4 3.8% 3.0% 3.7%

/ 1.7%

1.7% / 0.6% 0.6%

/ 0.8% /

0 MM-020 Rd Rd 18 MPT

2.4% 0.6% 1.1%

2.3% 0.6% 1.1%

1.9% 0.6% 0.9%

/

CVA 2.3% 2.0% / 0.9%

0.9% / CVA 1.4%

/ 0.3% MM-020 Rd Rd 18 MPT CVA

0.8% 0.6% 0.6% CVA

0.8% 0.6% 0.6% CVA 0.6% 0.6% 0.2%

[* MM–021 199

1 DVT

]

MM-009 MM-010

Stevens-Johnson

DRESS

/

-
-
-

PPP RMP

RMP

-
-
- RMP

- WCBP
-
-

RMP

-
-

24 24

-
- 4

4

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- 4
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-
-

4 4

- IUD

- (IUS)

  -)
-
-

-
-
-

4

4 6

25 mIU/mL

7

4

10 14 24

4 4

24

12 g/dl

-

8

- _____

_____

4

Rd Rd18 8.5% / / 15% 4

Rd Rd 18 0.6% / /

0.7%

Rd Rd 18 3 4

8.1% vs 11.1%

- _____

4

/ 5.1% /

0.6% 4 /

0.6% / 0.0%

3 4

/ 9.9% 1.4% /

2.3% 0.0%

TLS

TLS TFR CLL

TLS TLS TFR

TLS MDS

Stevens-Johnson

SJS TEN

DRESS DRESS

/

/

4 2 3

4

Stevens-Johnson DRESS

Lapp

-

1.38/100 - / 3.98/100 -

SPM

SPM { AML

MDS } 1.75/100 -

0.36/100 - 4.9

9 SPM

1.57/100 - 0.74/100 - 2.12

18

SPM 0.16/100 -

0.79/100 -

18

SPM 1.58/ 100 -

1.19/100 - 1.3

AML MDS B

1.31/100 - 0.58/100 - [

ASCT 1.02/100 - ASCT

0.60/100 -] SPM

1.36/100 - 1.05/100 - ASCT

1.26/100 - ASCT 0.60/100 -

ASCT

SPM

SPM

/

MPT

ASCT

3

HBV

HBV

HBV

HBV

HBc HBsAg

HBV

75 CLcr 60 mL/min

3 4

CLcr 60 mL/min

1:1

CLL

210 34

211 18 1.92[95%

: 1.08~3.41] 92% 2013 7

CLL

1

QTc 60 QT

2 QTc

90 CI 10 ms

3

4

0 17

MM-020 1613 94% 1521/1613
65 35% 561/1613 75 75
Rd 33% Rd 18 34% MPT 33% AE AE
3/4 AE AE 75

3/4 AE 5%

SOC 3 4 TEAE

5%

3/4 AE

AE

MM-009 MM-010 703

45% 5 12% /

/ / 353

46% /

65

CYP1A2 CYP2B6

CYP2C9 CYP2C19 CYP3A4/5

CYP3A4

10mg R- S-

25mg

PT

INR

10 mg/ 0.5 mg

14% 90%CI0.52%~28.2%

25 mg/ 40 mg/

P-gp

P- P-gp

P-gp 600 mg P-gp / 25

mg 25 mg

5

T T

CD34+

TNF- IL-6

Cullin ring E3 cereblon

[Cullin ring E3 DNA

DDB1 cullin 4 CUL4 cullins 1 Roc1] cereblon

—— Aiolos Ikaros

26 75 150 300mg/kg/ 3

NOAEL 75mg/kg/ AUC 25

20 4 6mg/kg/

1 1 2mg/kg/

/ 1mg/kg/

Ames

500mg/kg

25mg 200

-

AUC

MRHD 25mg 0.17 20

200

500mg/kg

25mg 200

-

7 20

20-40%

0.5 1.5 (C_{max})

(AUC)

S- R-

56% 44%

AUC

20% C_{max} 50%

[^{14}C]-

23% 29% 25mg/

0.01% 3

P150g/`qñ,,2ÏH9}ä0Öòuc$, õ×(¾s`ÄBsfEú" TÜ_-Õ Áÿ <P150g/`q ÐÖðLÙÑÒÃ. \vû’òd ñ

82%

N- 4.59% 1.83%

18

39 85

5 CLcr 56 74 mL/min 6

CLcr 33 46 mL/min 6 CLcr 17

29 mL/min 6 25 mg

7 CLcr 83 145 mL/min

25 mg

3 66% 75%

4.5 80%

4 30%

N = 16

AST > ULN

33 135

25mg 11 /

1

3 C_{max} AUC

10~30

6 / ×1 / 7 / ×3 /

24

YBH02832021

1 5mg H20213223

2 10mg H20213224

5

222069

4008285227 9:00-17:00

http://www.hansoh.cn