

|      |    |    |
|------|----|----|
| 2017 | 11 | 07 |
| 2019 | 02 | 21 |
| 2019 | 05 | 22 |
| 2019 | 05 | 24 |
| 2020 | 03 | 11 |
| 2020 | 12 | 11 |

®

Ustekinumab Injection

Wusinu Dankang Zhusheye

L-

L-

80

MTX

PUVA

A

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45mg/0.5ml/

90mg/1.0ml/

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45 mg

4

12

100 kg

100 kg

90 mg

4

12

45 mg

90 mg

28

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IV

1

8 90mg

12

90mg

1

|       |              |        |
|-------|--------------|--------|
|       | <sup>a</sup> | 130 mg |
|       | 260 mg       | 2      |
| 55 kg | 390 mg       | 3      |
| 85 kg | 520 mg       | 4      |

a 6 mg/kg

8

12

1

8

1

8

12

1

16

8

1

16

/

8

1

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45mg/0.5ml/

90mg/1.0ml/

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5%

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|     |       |       |       |       |  |    |     |       |
|-----|-------|-------|-------|-------|--|----|-----|-------|
| III | 5,884 | 4,135 | /     |       |  | 12 | II  | 1,749 |
| 6   | 4,105 | 1     | 2,846 |       |  |    |     |       |
|     |       |       | 4     | 1,482 |  | 5  | 838 |       |

2

|          |  |         |      |          |         |       |
|----------|--|---------|------|----------|---------|-------|
| 1/10     |  | 1/100   | 1/10 |          | 1/1,000 | 1/100 |
| 1/10,000 |  | 1/1,000 |      | 1/10,000 |         |       |

2

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|       |        |            |     |      |       |      |       |
|-------|--------|------------|-----|------|-------|------|-------|
| 1.38  |        |            |     | 1.35 |       |      |       |
|       |        | 0.03       |     | 829  |       | 27   |       |
|       | 0.03   |            | 385 |      | 11    |      |       |
|       |        |            |     |      |       |      | 5,884 |
|       |        | 10,953     |     |      | 0.99  |      |       |
|       | 3.2    |            |     | 1.0  |       |      |       |
| 0.6   |        |            |     | 0.91 |       |      |       |
| 0.02  |        | 10,953     |     | 178  |       |      |       |
| <hr/> |        |            |     |      |       |      |       |
|       |        |            |     |      | 0.12  | 100  |       |
| 829   |        | 1          |     | 0.26 | 100   |      | 385   |
|       | 1      |            |     |      |       |      | 0.48  |
| 100   |        | 829        |     | 4    |       | 0.52 | 100   |
|       | 385    |            | 2   |      |       |      |       |
| 5,884 |        | 10,935     |     |      |       | 1.0  |       |
|       | 3.2    |            |     |      | 1.0   |      |       |
| 0.6   | 10,935 |            |     |      |       |      | 58    |
|       |        |            |     | 0.53 | 100   |      |       |
|       |        | =0.87 [95% |     | 0.66 | 1.14] |      |       |
|       |        |            |     |      |       |      | 0.49  |
| 100   |        | 10,919     |     | 53   |       |      |       |
|       | 4:1    |            |     |      |       |      |       |
| <hr/> |        |            |     |      |       |      |       |

1%

466

2.4%

470

2.6%

1

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1

RPLS

12

RPLS

RPLS

RPLS

RPLS

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12.4%

3%

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/

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CT

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T

T cell enzyme-linked immune-spot assay T-SPOT.TB T

Quanti FERON-TB Gold QFT-G

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IL-12/IL-23

BCG

IL-12/IL-23

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60

PUVA

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[BCG]

15

2

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MTX

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1-3

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15

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/

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15

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18

---

65

65

65

III

100

5%

90%

MTX

NSAID

6-

IL-12

IL-23

CYP450

10 ng/ml

IL-12

/

IL-23

CYP450

CYP1A2

2B6

2C9

2C19

2D6

3A4

CYP450

IL-1 IL-6 \*ø ò.âjï-qÛ”.

|       |       |       |           |       |    |     |       |       |       |
|-------|-------|-------|-----------|-------|----|-----|-------|-------|-------|
| <hr/> |       |       |           |       |    |     |       |       |       |
|       | 2     |       |           |       |    |     |       |       | 1,996 |
| 1     |       |       |           |       |    |     |       | MTX   | PUVA  |
|       |       | 1     | PHOENIX 1 |       |    |     |       | 53%   |       |
|       |       |       |           | 766   |    |     |       |       | 0     |
| 4     | 45 mg | 90 mg |           | 12    |    |     |       |       |       |
|       |       | 0     | 4         |       |    | 12  | 16    |       |       |
|       |       | 45 mg | 90 mg     |       | 12 | 1   |       |       |       |
|       |       | 28    | 40        |       |    |     |       |       | PASI  |
| 75    | PASI  |       | 75%       |       |    |     |       | 12    | 1     |
|       |       |       |           | 40    |    |     |       |       |       |
|       |       | 40    | PASI      |       |    | 50% |       |       |       |
|       |       |       |           |       |    |     |       |       | 76    |
|       |       | 2     | PHOENIX 2 |       |    |     |       | 61%   |       |
|       |       |       |           | 1,230 |    |     |       |       | 0     |
| 4     | 45 mg | 90 mg |           | 16    |    |     | 1     |       |       |
|       |       | 0     | 4         |       |    | 12  | 16    |       |       |
|       |       | 45 mg | 90 mg     |       |    |     |       |       | 52    |
|       |       | 3     | ACCEPT    |       |    |     |       |       |       |
|       |       |       |           | 903   |    |     |       |       |       |
|       |       |       |           |       | 12 |     |       |       |       |
| 2     | 50 mg |       | 0         | 4     |    |     | 45 mg | 90 mg |       |

1 2 PASI  
 17-18 BSA 20  
 DLQI 10-12 1/3 1 1/4 2  
 PsA 3  
 12 PASI 75  
 3 4  
 3 1 PHOENIX 1 2 PHOENIX 2

|                  |          | 12       |                        | 28                     |           |
|------------------|----------|----------|------------------------|------------------------|-----------|
|                  |          | 2        | 0                      | 4                      | 3         |
|                  |          |          |                        |                        | 0         |
|                  |          |          |                        | 4                      | 16        |
|                  |          |          | 45 mg                  | 90 mg                  | 45 mg     |
|                  |          |          |                        |                        | 90 mg     |
|                  | <b>1</b> |          |                        |                        |           |
|                  |          | 255      | 255                    | 256                    | 250       |
| PASI 50          | %        | 26 (10%) | 213 (84%) <sup>a</sup> | 220 (86%) <sup>a</sup> | 228 (91%) |
| PASI 75          | %        | 8 (3%)   | 171 (67%) <sup>a</sup> | 170 (66%) <sup>a</sup> | 178 (71%) |
| PASI 90          | %        | 5 (2%)   | 106 (42%) <sup>a</sup> | 94 (37%) <sup>a</sup>  | 123 (49%) |
| PGA <sup>b</sup> | %        | 10 (4%)  | 151 (59%) <sup>a</sup> | 156 (61%) <sup>a</sup> | 146 (58%) |
| 100 kg           |          | 166      | 168                    | 164                    | 164       |
| PASI 75          | %        | 6 (4%)   | 124 (74%)              | 107 (65%)              | 130 (79%) |
| 100 kg           |          | 89       | 87                     | 92                     | 86        |
| PASI 75          | %        | 2 (2%)   | 47 (54%)               | 63 (68%)               | 48 (56%)  |
|                  | <b>2</b> |          |                        |                        |           |
|                  |          | 410      | 409                    | 411                    | 397       |
| PASI 50          | %        | 41 (10%) | 342 (84%) <sup>a</sup> | 367 (89%) <sup>a</sup> | 369 (93%) |
|                  |          |          |                        |                        | 380 (95%) |

|                  |   |         |                        |                        |           |           |
|------------------|---|---------|------------------------|------------------------|-----------|-----------|
| PASI 75          | % | 15 (4%) | 273 (67%) <sup>a</sup> | 311 (76%) <sup>a</sup> | 276 (70%) | 314 (79%) |
| PASI 90          | % | 3 (1%)  | 173 (42%) <sup>a</sup> | 209 (51%) <sup>a</sup> | 178 (45%) | 217 (54%) |
| PGA <sup>b</sup> |   | 18 (4%) | 277 (68%) <sup>a</sup> | 300 (73%) <sup>a</sup> | 241 (61%) | 279 (70%) |
|                  | % |         |                        |                        |           |           |
| 100 kg           |   | 290     | 297                    | 289                    | 287       | 280       |
| PASI 75          | % | 12 (4%) | 218 (73%)              | 225 (78%)              | 217 (76%) | 226 (81%) |
| 100 kg           |   | 120     | 112                    | 121                    | 110       | 119       |
| PASI 75          | % | 3 (3%)  | 55 (49%)               | 86 (71%)               | 59 (54%)  | 88 (74%)  |

<sup>a</sup> 45 mg 90 mg p 0.001

<sup>b</sup> PGA=

4 3 ACCEPT 12

|         | 3         |                        |                        |
|---------|-----------|------------------------|------------------------|
|         | 24        | 2                      | 0 4                    |
|         |           | 2<br>50mg              | 45 mg                  |
|         | 347       | 209                    | 347                    |
| PASI 50 | 286 (82%) | 181 (87%)              | 320 (92%) <sup>a</sup> |
| PASI 75 | 197 (57%) | 141 (67%) <sup>b</sup> | 256 (74%) <sup>a</sup> |
| PASI 90 | 80 (23%)  | 76 (36%) <sup>a</sup>  | 155 (45%) <sup>a</sup> |
| PGA     | 170 (49%) | 136 (65%) <sup>a</sup> | 245 (71%) <sup>a</sup> |
|         | %         |                        |                        |
| 100 kg  | 251       | 151                    | 244                    |
| PASI 75 | 154 (61%) | 109 (72%)              | 189 (77%)              |

|         |   |          |          |
|---------|---|----------|----------|
| 100 kg  |   | 96       | 58       |
| PASI 75 | % | 43 (45%) | 32 (55%) |

<sup>a</sup> 45 mg 90 mg p 0.001

<sup>b</sup> 45 mg p=0.012

p 0.001 1 PASI 75 1 52  
 52 Xf1P52M1WVWPRTSx000P11 B h  
 52



1409      UNITI-1 n=769    UNITI-2 n=640  
6      CDAI  
8      75%  
0  
6 mg/kg      1      130 mg

UNITI-1      48%  
1    TNF      52%      2    3  
29.1%      36.4%      69.4%

UNITI-2  
68.6%  
31.4%

UNITI-1    UNITI-2  
5      3  
8  
130 mg

5    UNITI-1    UNITI-2

|   |     | UNITI-1*   |                         | UNITI-2**  |                          |
|---|-----|------------|-------------------------|------------|--------------------------|
|   |     | N=247      | N=249                   | N=209      | N=209                    |
| 8 |     | 18 (7.3%)  | 52 (20.9%) <sup>a</sup> | 41 (19.6%) | 84 (40.2%) <sup>a</sup>  |
| 6 | 100 | 53 (21.5%) | 84 (33.7%) <sup>b</sup> | 60 (28.7%) | 116 (55.5%) <sup>a</sup> |

|    |     |            |                          |            |                          |
|----|-----|------------|--------------------------|------------|--------------------------|
| 8  | 100 | 50 (20.2%) | 94 (37.8%) <sup>a</sup>  | 67 (32.1%) | 121 (57.9%) <sup>a</sup> |
| 70 | 3   | 67 (27.1%) | 101 (40.6%) <sup>b</sup> | 66 (31.6%) | 106 (50.7%) <sup>a</sup> |
| 70 | 6   | 75 (30.4%) | 109 (43.8%) <sup>b</sup> | 81 (38.8%) | 135 (64.6%) <sup>a</sup> |

CDAI                      150                      CDAI

100

70                      CDAI                      70

\*

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<sup>a</sup> p 0.001

<sup>b</sup> p 0.01

IM-UNITI                      UNITI-1      UNITI-2

8                      100                      388

90 mg                      8                      90 mg                      12

44

44

6

6 IM-UNITI                      44                      52

|  |                         |                                       |                                     |
|--|-------------------------|---------------------------------------|-------------------------------------|
|  | *<br>N=131 <sup>†</sup> | 90 mg<br>8<br>1<br>N=128 <sup>†</sup> | 90 mg<br>12 1<br>N=129 <sup>†</sup> |
|  | 36%                     | 53% <sup>a</sup>                      | 49% <sup>b</sup>                    |
|  | 44%                     | 59% <sup>b</sup>                      | 58% <sup>b</sup>                    |
|  | 30%                     | 47% <sup>a</sup>                      | 43% <sup>c</sup>                    |
|  |                         |                                       |                                     |

|         |   |             |                          |             |
|---------|---|-------------|--------------------------|-------------|
|         |   | 46% (36/79) | 67% (52/78) <sup>a</sup> | 56% (44/78) |
| CRD3002 | † | 44% (31/70) | 63% (45/72) <sup>c</sup> | 57% (41/72) |
|         |   | 49% (25/51) | 65% (34/52) <sup>c</sup> | 57% (30/53) |
| CRD3001 | § | 26% (16/61) | 41% (23/56)              | 39% (22/57) |

CDAI 150 CDAI  
 100  
 \*  
 † 100  
 ‡  
 § /  
<sup>a</sup> p 0.01  
<sup>b</sup> p 0.05  
<sup>c</sup> p 0.05  
 IM-UNITI 29/129 12 1  
 8 1  
 CDAI 220 CDAI 100  
 41.4% 16  
 UNITI-1 UNITI-2 8  
 476 IM-UNITI  
 90 mg 8 50.5%  
 8 44  
 68.1% 50.2%  
 131 51 90 mg  
 8 1  
 24 51 70.6%  
 16 39.2%

IM-UNITI 44  
 TNF 92

252  
 SES-CD /

5 /

8 n=155 = -2.8

SES-CD n=97 = -0.7 p=0.012

8.8% n=26 12/15 80%

44  
 50% 45.5% 5/11

IBDQ SF-36 8  
 UNITI-1 UNITI-2 IBDQ SF-  
 36 UNITI-2 SF-36 44 IM-UNITI

p40 IL-12 IL-23  
 IL-12 IL-23  
 CD<sup>4+</sup>T  
 IL-12R  
 IL-12 IL-23

IL-12 IL-23 p40

|                |       |                 |           |     |                        |
|----------------|-------|-----------------|-----------|-----|------------------------|
| 45             |       | 45mg/kg         | mg/kg     |     | 2                      |
| IL-12/IL-23p40 |       |                 | 50mg/kg   |     | 2                      |
| 1              | -     |                 |           | 2   | 100                    |
| 90mg           |       | 4               |           | 100 |                        |
| 1              |       | 33              |           | 2   |                        |
|                |       | 100             | 22.5mg/kg | 1   | 45mg/kg                |
|                |       |                 | 6         |     |                        |
| 12             |       | IL-12/IL-23 p40 |           |     | IL-<br>IL-12/IL-23 p40 |
| IL-12          | IL-23 |                 | IL-12     |     |                        |

|                   |         |      |       |       |                 |
|-------------------|---------|------|-------|-------|-----------------|
|                   | 26      |      | 10    |       | 26              |
|                   | 45mg/kg | 1    |       |       |                 |
| 8.5               |         |      | 90 mg |       | $T_{max}$       |
|                   |         |      | 45 mg | 90 mg | $T_{max}$       |
|                   |         |      |       |       | 57.2%           |
| ml/kg             |         |      |       | $V_z$ | 57~83           |
| 1.99~2.34 ml/ /kg |         |      |       |       | CL              |
| $t_{1/2}$         |         | 3    | 15~32 |       |                 |
|                   |         | CL/F |       | V/F   | 0.465 L/ 15.7 L |
| $t_{1/2}$         |         | 3    |       | CL/F  |                 |

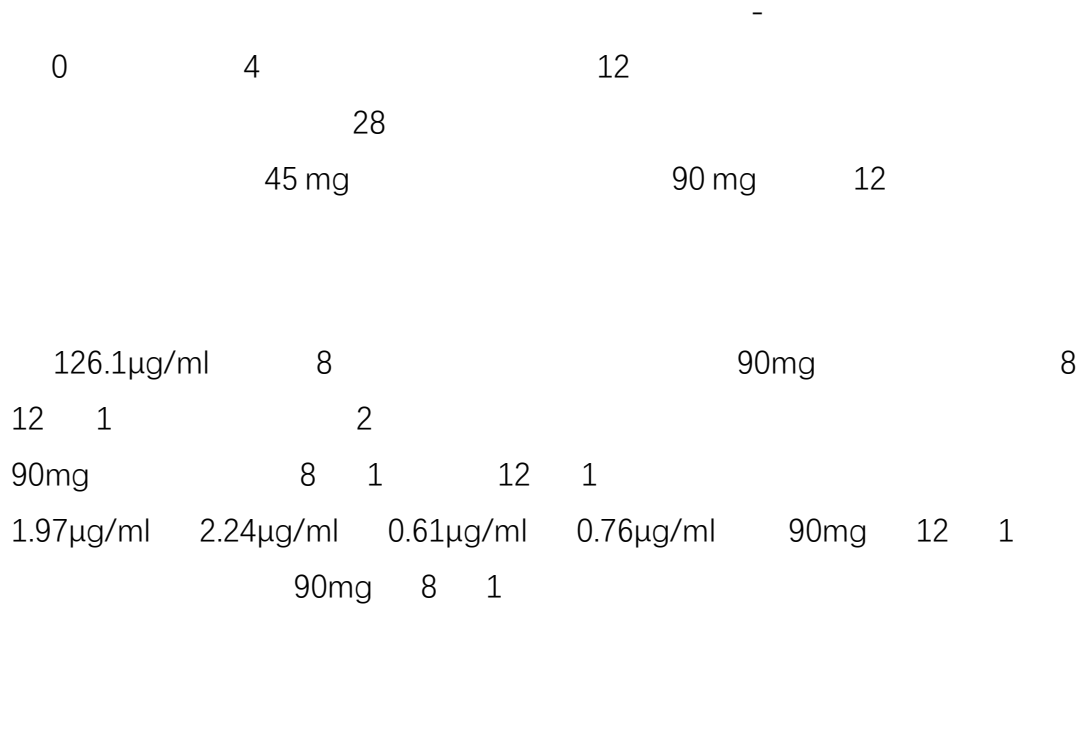
0.09 mg/kg~4.5 mg/kg

24 mg~240 mg

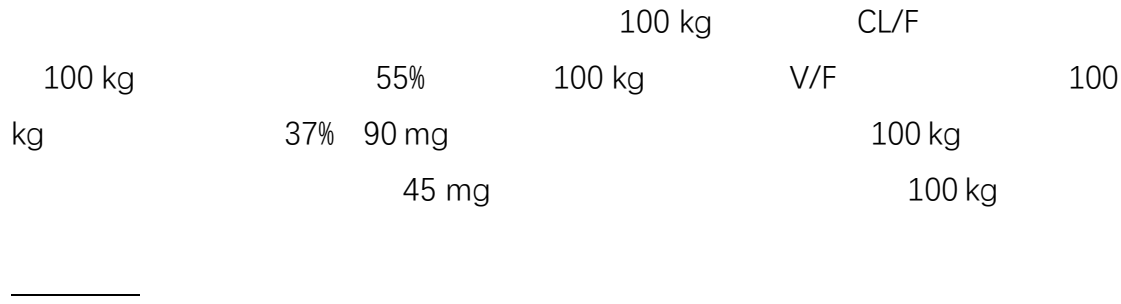
C<sub>max</sub>

AUC

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CL/F V/F

65

12-17

CYP450

|        |     |     |          |       |       |       |        |
|--------|-----|-----|----------|-------|-------|-------|--------|
|        |     |     |          |       | IL-12 | IL-23 | CYP450 |
|        |     |     | 10 ng/ml | IL-12 | /     | IL-23 | CYP450 |
| CYP1A2 | 2B6 | 2C9 | 2C19     | 2D6   | 3A4   |       |        |

2~8

1ml I  
1  
1 /  
36

JS20180014

45mg/0.5ml/ S20170047

90mg/1.0ml/ S20170046

Janssen-Cilag International NV  
Turnhoutseweg 30, B-2340 Beerse, Belgium



Cilag AG

Hochstrasse 201, 8200 Schaffhausen, Switzerland

19

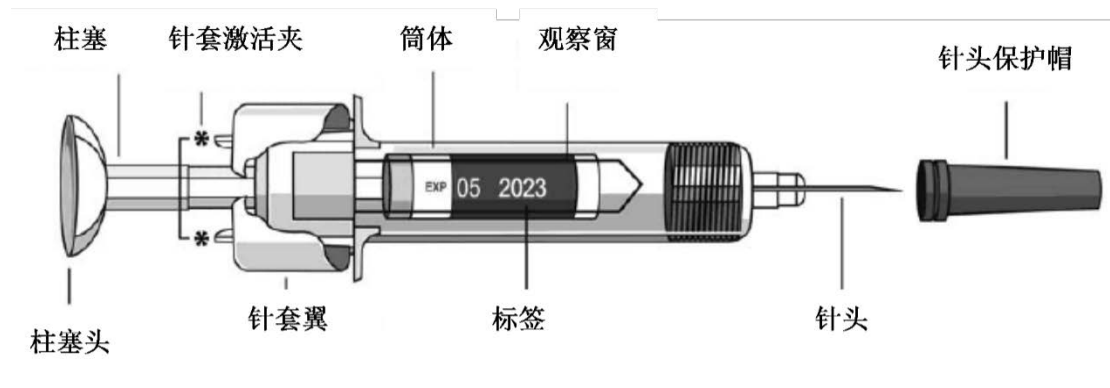
710304

400 888 9988

(029)82576616

<http://www.xian-janssen.com.cn>

1



1

1.

1

\*

45 mg/0.5 ml/

- 45 mg 45 mg
- 90 mg 45 mg

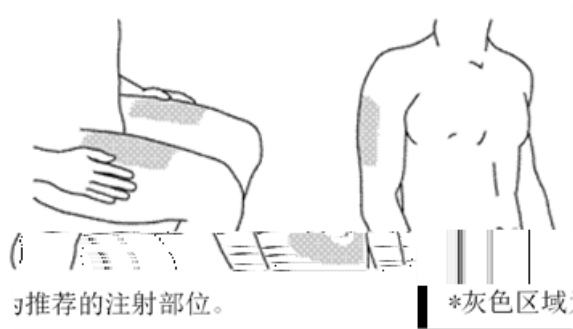
90 mg/1.0 ml/

- 90 mg 90 mg

2.

2

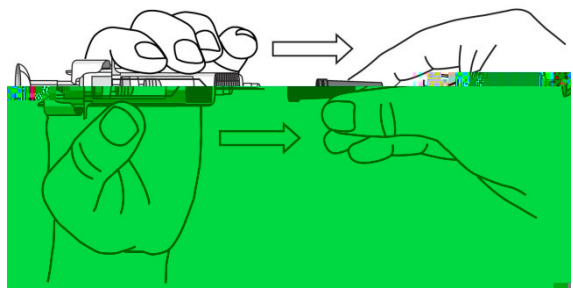
5 cm



2

3.

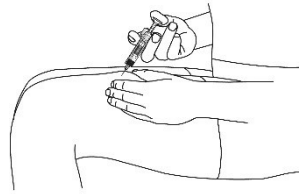
3



3

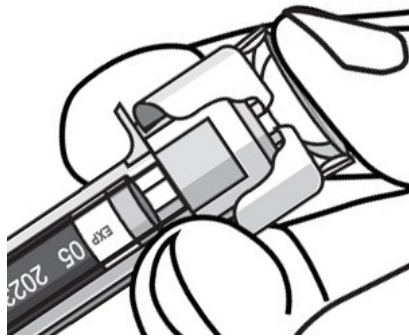
4.

4



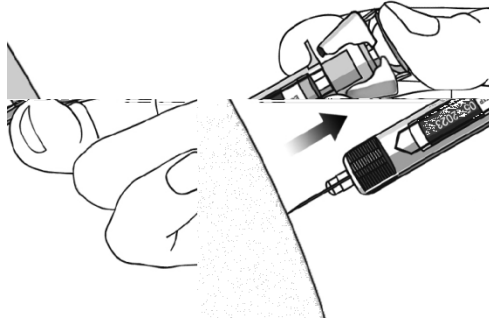
4

5



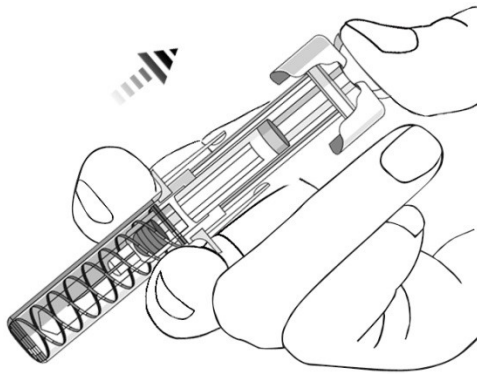
5

6



6

7

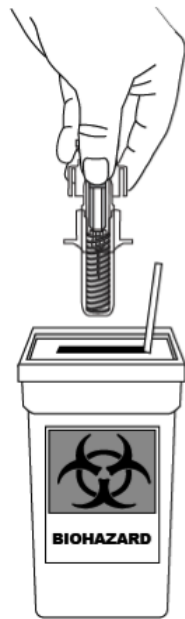


7

5.

6.

8



8