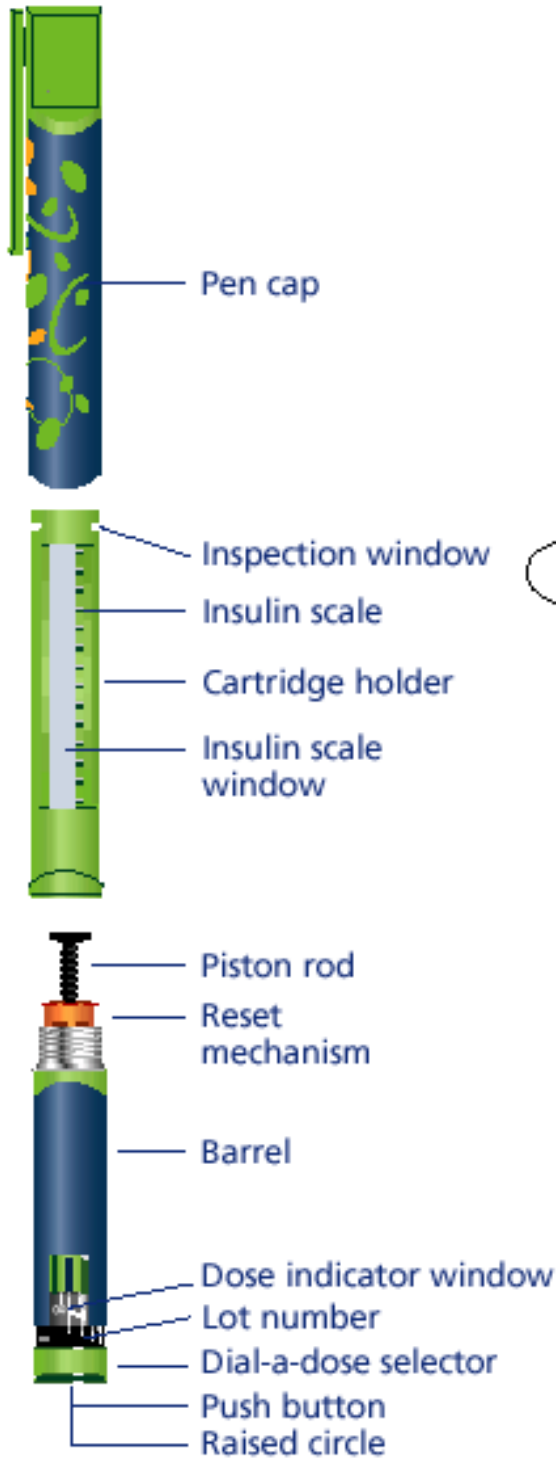
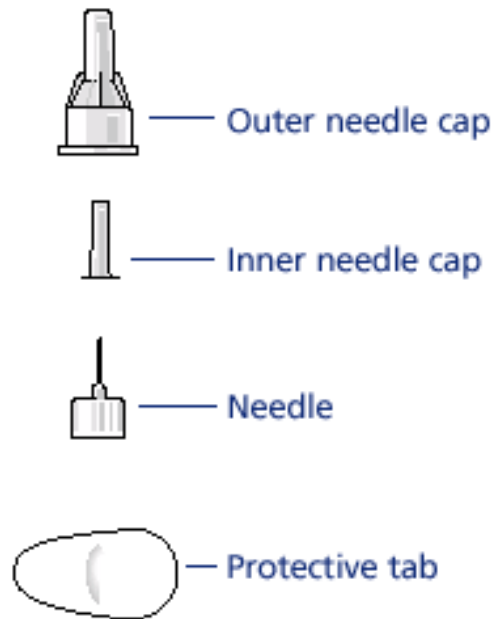


Open this flap
for drawings of the
NovoPen® Junior
insulin injection system

NovoPen® Junior Insulin Delivery Device



NovoFine® Disposable Needle



PenFill® Cartridge (3 mL)



Need Help?
Call 1-800-727-6500

4

5

NovoPen[®] Junior Instruction Manual

6

7

8

Dial-A-Dose Insulin Delivery System

9

10

INTRODUCTION

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15

NovoPen[®] Junior delivers a minimum dose of 1 unit to a maximum dose of 35 units of insulin in half unit steps. A raised circle on the push button makes it easy for you to know your NovoPen Junior from the ordinary NovoPen 3. This booklet includes everything you need to know about using the NovoPen Junior. Please read it carefully before using your NovoPen Junior for the first time.

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20

The NovoPen Junior is designed for use with:

21

22

23

- PenFill[®] 3 mL cartridges.
- NovoFine[®] disposable needles.

24

NovoFine disposable needles are for single-use only.

25

You will also need alcohol swabs.

26

27

If you have any questions about your NovoPen Junior insulin delivery system, please call Novo Nordisk Pharmaceuticals, Inc. at 1-800-727-6500.

28

29

30

Please complete and return the NovoPen Junior warranty card.

31

32

33

34

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See **Important Things to Know** and **Important Notes** on pages 33-35.

36

37

38 **HOW TO USE THIS BOOKLET**

39

40 **This booklet gives you step-by-step instructions for using the NovoPen**
41 **Junior.**

42

43 Begin by reviewing the drawing layout of the parts of the NovoPen Junior, PenFill
44 3 mL cartridge, and NovoFine disposable needle. The inside front cover opens
45 out so you have a handy reference while you read the rest of the booklet.

46

47 Most pages contain a drawing on the right with numbered instructions to the left
48 of the drawing.

49 **Important additional information is given below the drawing.**

50

51 We suggest that you **read the text and look at the drawing** to make sure that
52 you understand each step thoroughly.

53

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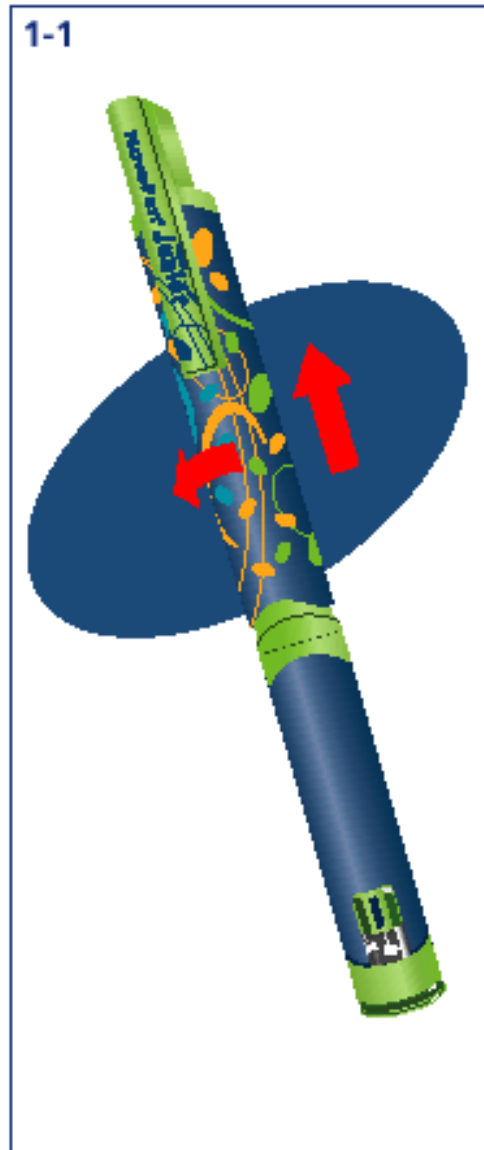
81

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83		
84	SECTION 1:	
85	Preparing the NovoPen Junior.....	5
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88	Inserting the PenFill 3 mL Cartridge.....	8
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119 **SECTION 1** **Preparing the NovoPen Junior**
120

121 **Remove the device cap:**

- 122 1. Remove the NovoPen Junior from the case.
123 2. Gently twist the pen cap until the cap separates from the barrel.
124 3. Pull the pen cap straight up to remove it.
125



Need Help?
Call 1-800-727-6500

126
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128 **If you use more than one insulin product (such as Novolin® R, Novolin® N,**
129 **Novolin® 70/30, or NovoLog®), use a separate insulin delivery device for each**
130 **product.**

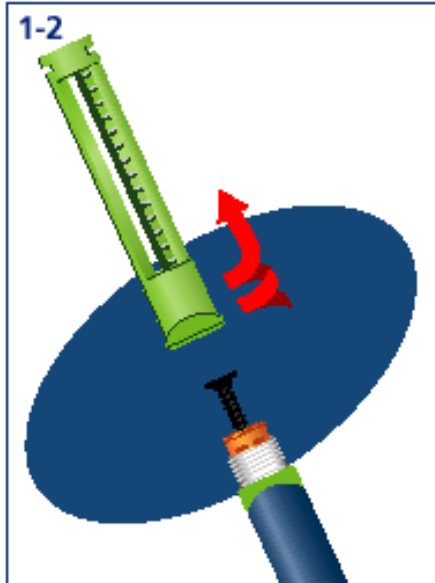
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SECTION 1 (cont.)

Separate the cartridge holder from the barrel:

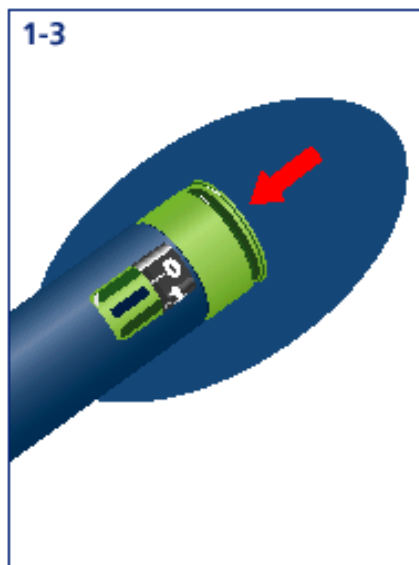
4. Unscrew and remove the cartridge holder from the barrel.



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Make sure the dose indicator window shows zero:

5. Press the push button all the way in until zero (0) appears in the window.
The zero should be lined up with the stripe below the dose indicator window.



147

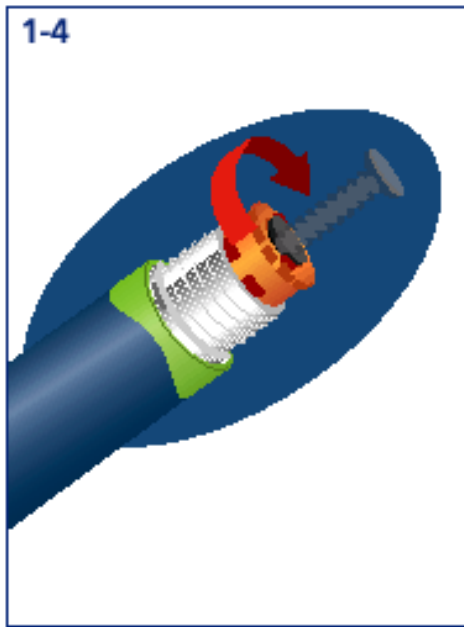
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SECTION 1 (cont.)

The end of the piston rod should be flat against the end of the reset mechanism prior to inserting each new PenFill 3 mL cartridge. It should not be sticking out.

If the piston rod is sticking out:

Turn the end of the reset mechanism in a clockwise direction until it is no longer sticking out. Never push the piston rod back in.



160



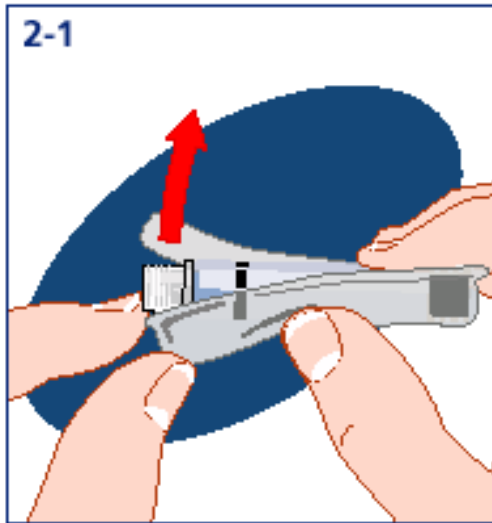
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You should never reset the piston rod until it is time to remove the used PenFill 3 mL cartridge and insert a new one.

If the reset mechanism locks, it is usually due to improper technique. Gently turn the mechanism side to side until it unlocks. Then call our toll free number (1-800-727-6500) so that we may go over your technique with you.

171 **SECTION 2 Inserting the PenFill 3 mL Cartridge**
172

- 173 1. To remove the PenFill cartridge from its wrapper, push the cartridge
174 through the foil side of the packaging. Always make sure that the PenFill
175 cartridge you use contains the correct type of insulin (such as Novolin R,
176 Novolin N, Novolin 70/30, or NovoLog). If you are treated with more than
177 one type of insulin in PenFill cartridges, you should use a separate insulin
178 delivery device for each type of insulin. Before use, check that the PenFill
179 cartridge is full and intact. If not, do not use it.
180



- 181
182
183 2. In the PenFill Information For The Patient leaflet, you will find instructions
184 on how to prepare the insulin if the PenFill contains a suspension insulin
185 (white and cloudy insulin) such as Novolin N or Novolin 70/30.
186
187

188 Each PenFill 3 mL cartridge contains a total of 300 units of insulin. Make sure
189 you are using the correct type of insulin. On the glass part of the cartridge is the
190 name of the insulin.

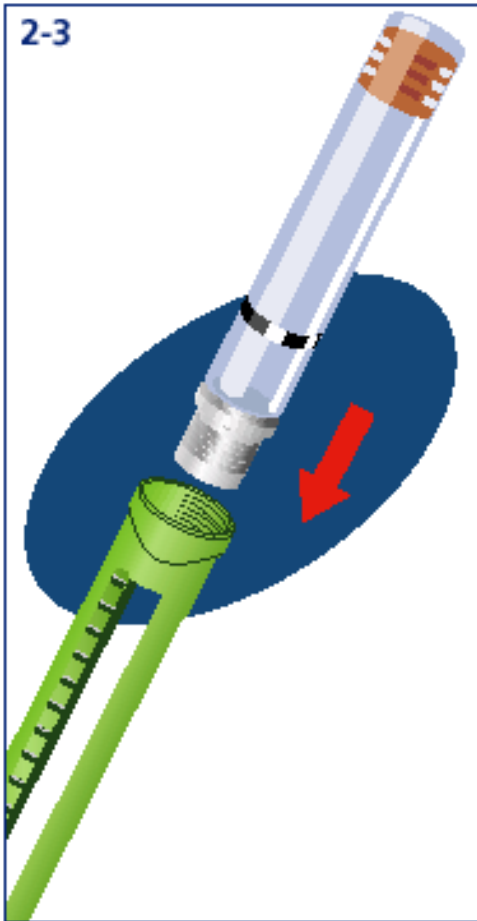
191
192 Each PenFill cartridge is for single-person use only. **DO NOT** share the same
193 cartridge with anyone even if you attach a new disposable needle for each
194 injection. Sharing the cartridge can spread disease.
195 Use only a new PenFill 3 mL cartridge when loading the NovoPen Junior. Never
196 load a partially filled cartridge.
197 Never try to refill a used PenFill 3 mL cartridge.
198
199

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SECTION 2 (cont.)

Insert the PenFill cartridge:

2. Hold the cartridge holder so the wider opening is up.
3. Drop the PenFill cartridge into the cartridge holder, plastic cap first.



208
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214

A threaded plastic cap surrounds the end of the PenFill® cartridge, like the cap on a bottle. In the center is the front rubber stopper.
The rear rubber stopper is at the other end of the PenFill cartridge.

215 **SECTION 2 (cont.)**

216

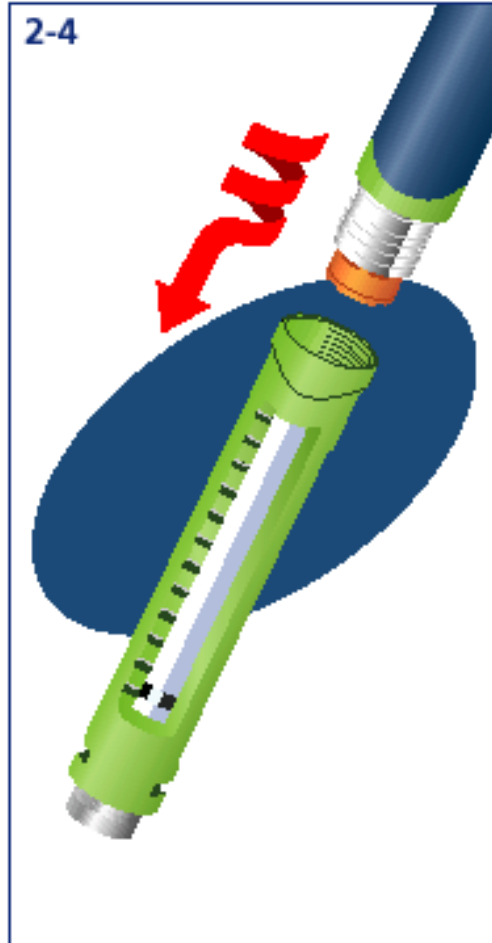
217 **Re-attach the cartridge holder:**

218

219

220

4. Screw the barrel into the cartridge holder completely until it is tight.



Need Help?
Call 1-800-727-6500

221

222

223

224

225 You can see the cartridge in the insulin scale window. The cartridge holder has a
226 scale with marks showing about how much insulin is left in the PenFill cartridge.

227

228

229

230 **SECTION 3 Attaching the NovoFine® Disposable Needle**

231

232 At the end of the cartridge holder are two inspection windows. You can see the
233 cartridge through these windows.

234

235 **If you use a suspension insulin (white and cloudy) such as Novolin® N or**
236 **Novolin® 70/30, use the windows to check if there is enough insulin left for**
237 **proper mixing.** (see below)

238

239 **Check the amount of insulin remaining:**

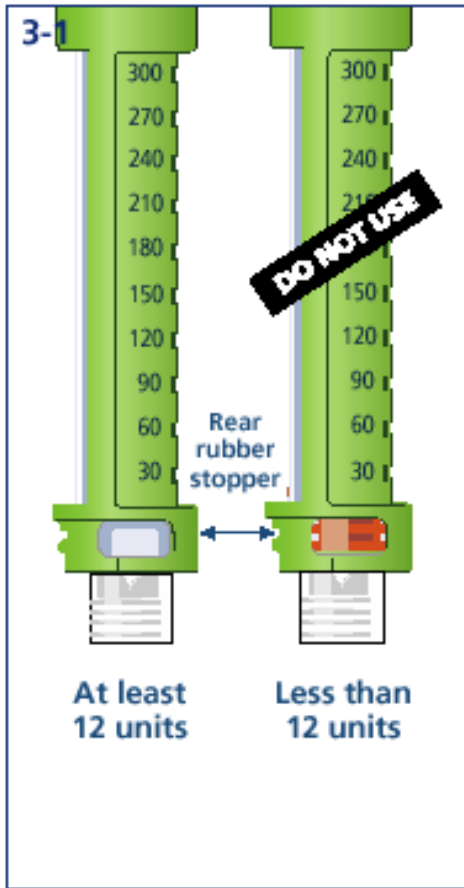
240

- 241 ▪ If the rear rubber stopper cannot be seen in the inspection window, you
- 242 have enough insulin for mixing left in the cartridge.
- 243 ▪ If the rear rubber stopper can be seen in the inspection window, you do
- 244 not have enough insulin left in the cartridge and must insert a new PenFill
- 245 3 mL cartridge.

246

247 See Section 7 for instructions on removing a PenFill cartridge and Section 2 for
248 inserting a new one.

249



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251 12

252 **SECTION 3 (cont.)**

253

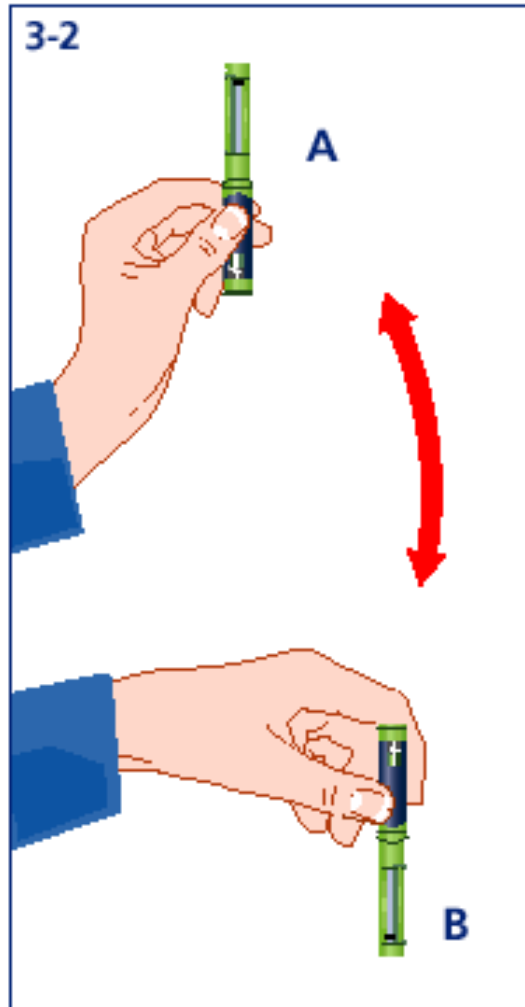
254 **For users of suspension insulin (white and cloudy) such as Novolin N or**
255 **Novolin 70/30:**

256

257 **Always remix the insulin before each injection.**

258 To remix the insulin, turn the NovoPen Junior up and down between positions **A**
259 and **B** 10 times or until the insulin looks uniformly white and cloudy

260



Need Help?
Call 1-800-727-6500

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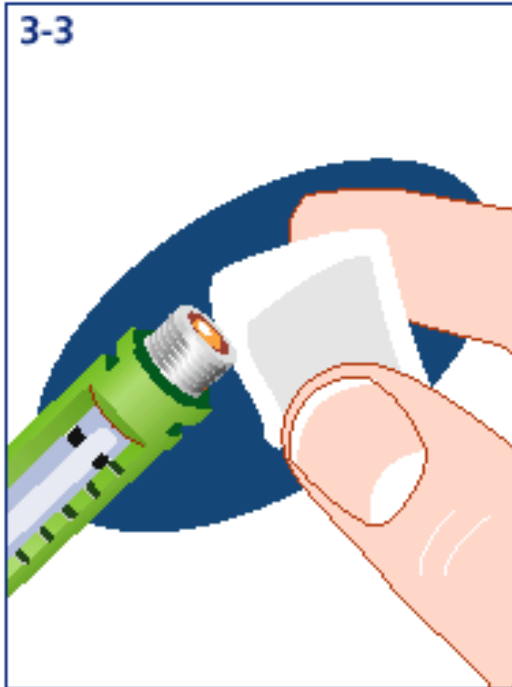
265 **SECTION 3 (cont.)**

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268

1. Wipe the front rubber stopper with an alcohol swab.



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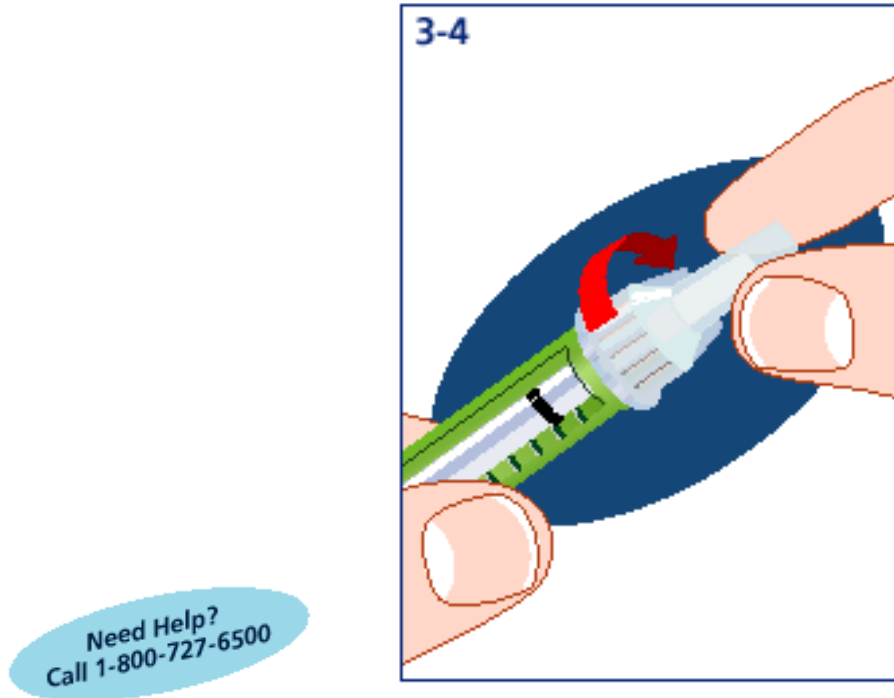
274

You must wipe the front rubber stopper with an alcohol swab before each injection, even if you are using the same PenFill cartridge.

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SECTION 3 (cont.)

2. Remove the protective tab from the NovoFine disposable needle.
3. Screw the NovoFine disposable needle firmly onto the PenFill 3 mL cartridge until it is tight.



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288

Never place a NovoFine disposable needle on your NovoPen Junior until you are ready to do an air shot and give an injection. If the NovoFine needle is left on, some liquid may leak out of the PenFill cartridge. This may cause a change in the strength of the suspension insulin such as Novolin N or Novolin 70/30.

289

290 **SECTION 4 Doing an Air Shot**

291

292 The PenFill cartridge may contain an air bubble, and small amounts of air may
293 collect in the needle and PenFill cartridge when you use them. To avoid injecting
294 air and to ensure proper dosing, you must perform an air shot before each
295 injection.

296

297 **Before doing the air shot, the dose indicator window must show zero (0).**

298

299 If you use a suspension insulin, such as Novolin N or Novolin 70/30 and have
300 used the PenFill cartridge for previous injections, make sure there is enough
301 insulin left in the PenFill cartridge to properly mix the insulin (see page 12). If
302 there is enough insulin left in the PenFill cartridge, see the next page for
303 instructions.

304

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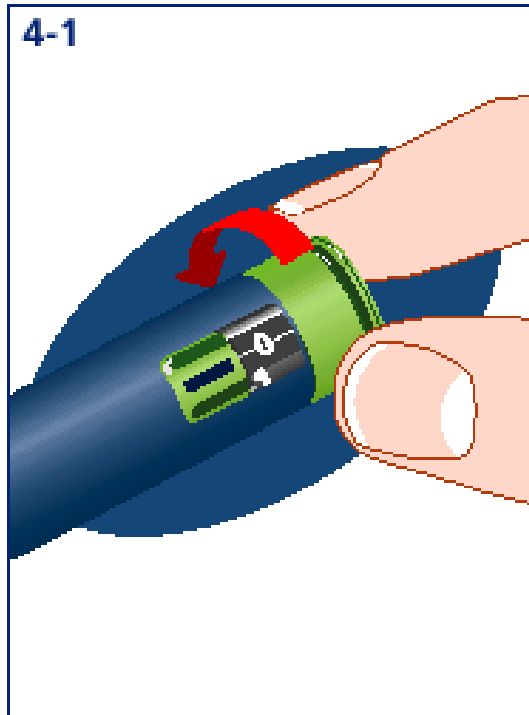
306 **SECTION 4 (cont.)**

307

308 **Set the NovoPen Junior for the air shot:**

309

- 310 1. Turn the dial-a-dose selector to 2 units. Full units are shown as numbers.
311 Half units are shown as long lines between the numbers.
312



Need Help?
Call 1-800-727-6500

313

314

315 **If you dial more than 2 units, DO NOT turn the dial back to zero (0).** If you
316 do, the extra insulin will squirt out of the needle. You may complete the air shot
317 with the number of units you have dialed or refer to Section 5 on page 21 for
318 instructions on how to reset the dose to zero.

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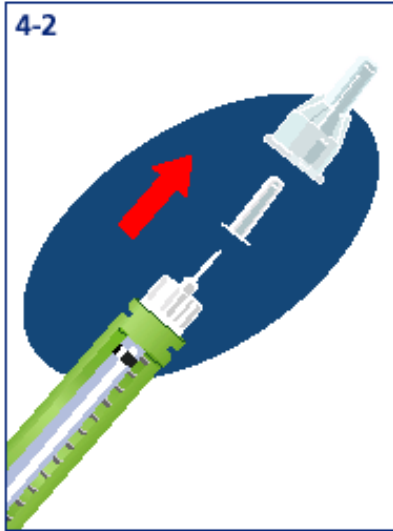
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SECTION 4 (cont.)

Uncap the NovoFine needle:

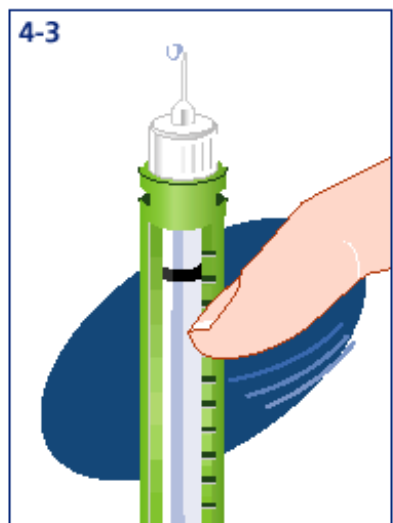
2. Pull off the outer needle cap and set aside.
3. Pull off the inner needle cap and discard.

Do not use the needle if it is bent or damaged.



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4. Hold the NovoPen Junior with the NovoFine needle pointing up.
5. Tap the cartridge holder with your finger a few times to raise any air bubbles that may be present to the top of the cartridge.



336
337
338

339 **SECTION 4 (cont.)**

340

341 **Do the air shot:**

342

343 6. Press the push button all the way in. A drop of insulin should appear at the
344 needle tip.

345

346 **If no insulin appears, repeat the following steps, until a drop of insulin**
347 **appears:**

348

349 a. Make sure the NovoFine needle is securely attached.

350

b. Dial 2 units.

351

c. Tap the cartridge holder with your finger.

352

d. Press the push button all the way in.

353

354 There may still be some small air bubble(s) in the PenFill cartridge after this, but
355 they will not affect your dose and they will not be injected.

356

Need Help?
Call 1-800-727-6500



357

358

359 When you press the push button, the piston rod presses against the rear rubber
360 stopper. This moves the rear rubber stopper and pushes the correct amount of
361 insulin up through the needle.

362

364 **SECTION 5 Giving the Injection**

365

366 **Be sure to do an air shot before giving each injection (see pages 16-19).**

367

Select the dose:

368

369

- 1 Check that the dial-a-dose selector is set to zero. If not, follow the instructions on the next page. Turn the dial-a-dose selector until you see the correct number of units in the dose indicator window. Full units are shown as numbers. Half units are shown as long lines between the numbers.

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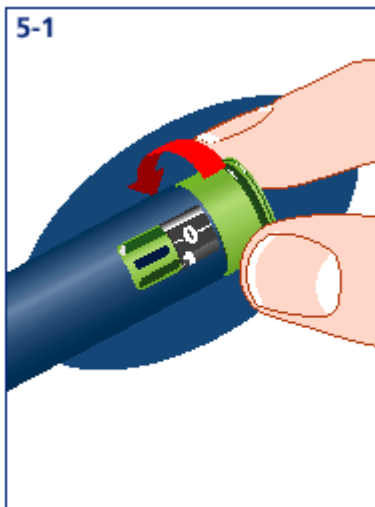
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DO NOT use the clicking sound as a guide for selecting your dose.

376



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379 The NovoPen Junior can deliver insulin in half unit steps from a minimum dose
380 of 1 unit to a maximum dose of 35 units.

381

382 **If you dial more than your dose, DO NOT turn the dial back to zero (0).** If you
383 do, the extra insulin will squirt out of the needle. For instructions on how to reset
384 the dose to zero (0) so you can start again, see the next page.

385

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387

388 **SECTION 5 (cont.)**

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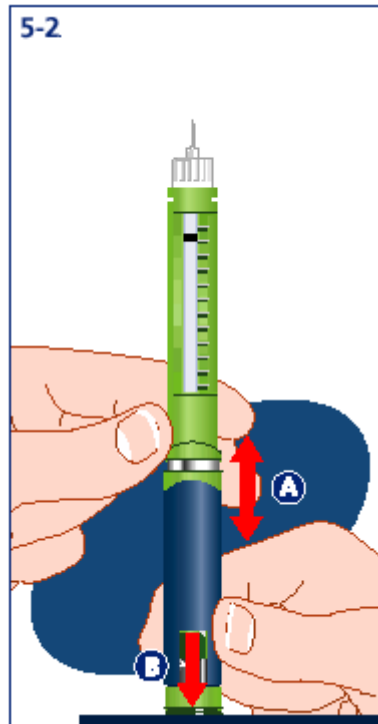
390 If you dial a larger dose than you need, pull the barrel and the cartridge holder
391 apart, as shown in the drawing **A**. While holding them apart, gently press the
392 push button against a hard surface and release your grip **B**. Your dose indicator
393 window should be back to zero (0).

394

395 You can now dial the correct number of units.

396

Need Help?
Call 1-800-727-6500



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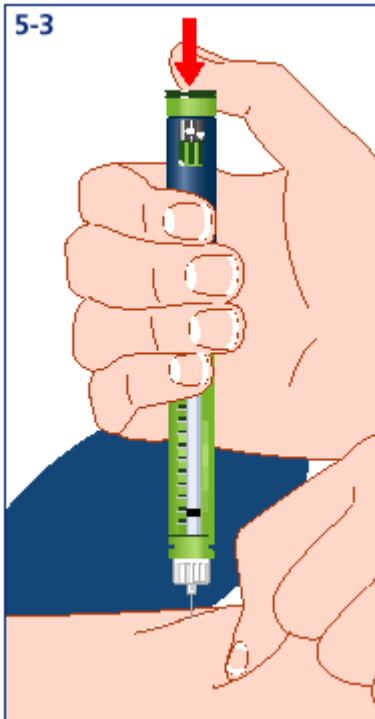
SECTION 5 (cont.)

Giving the injection:

2. After the air shot is done and you have chosen the correct number of units, insert the NovoFine needle in the correct injection site on your body. (Use the injection technique recommended by your health care professional). If you use a suspension insulin such as Novolin N or Novolin 70/30, mix the insulin (see page 13, Section 3) and make sure the insulin looks uniformly white and cloudy before you inject.
3. Press the push button **as far as it will go** to deliver the insulin. Do not force it.

To ensure that all the insulin is injected, keep the NovoFine needle in the skin for several seconds after injection with your thumb on the push button. Keep the push button fully depressed until after the NovoFine needle has been withdrawn.

Important: Never turn the dial-a-dose selector to inject the insulin.



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When you get near the end of a PenFill cartridge, you may need to give yourself two injections to receive your full dose. Check the dose indicator window after giving an injection. If zero does not appear in the dose indicator window, you did

426 not receive your full dose. See the next page for instructions on how to get the
427 remaining part of your dose.

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SECTION 5 (cont.)

4. Check the dose indicator window to make sure it shows zero (0). If zero does not appear, you did not receive the full dose.

If the dose indicator window does not show zero, there were not enough units of insulin in the PenFill cartridge for you to receive the full dose. The dose indicator window shows the number of units that you did not receive.

For example, if you dial **25** units and there are only **20** units left in the PenFill cartridge, after the injection the number in the dose indicator window will be **5** ($25-20 = 5$). If this happens, proceed with the following steps to get the remaining part of your dose:

- a. Note the number of units in the dose indicator window.
- b. Remove the NovoFine needle (see Section 6).
- c. Remove the empty PenFill 3 mL cartridge (see Section 7).
- d. Insert a new PenFill 3 mL cartridge (see Section 2).
- e. Attach a NovoFine needle (see Section 3).
- f. Do an air shot (see Section 4).
- g. Dial the number of units noted in step a.
- h. Give the injection.



455
456
457

458 **SECTION 6 Removing the NovoFine Disposable Needle**

459
460 **Remove the NovoFine disposable needle:**

- 461
- 462 1. After the injection, remove the needle without replacing the cap.
 - 463
 - 464 2. Hold the cartridge holder firmly while you unscrew the NovoFine
 - 465 disposable needle.
 - 466
 - 467 3. Place the NovoFine disposable needle in a puncture-resistant disposable
 - 468 container.
 - 469

470 Health care professionals, relatives and other caregivers should also follow the
471 above instructions to eliminate the risk of unintended needle penetration.
472

473
474
475
476 **The NovoFine disposable needle must be removed immediately after each**
477 **injection without replacing the cap.** If the NovoFine disposable needle is not
478 removed, some liquid may leak out of the PenFill cartridge. This may cause a
479 change in the strength of suspension insulins (white and cloudy) such as Novolin
480 N or Novolin 70/30.

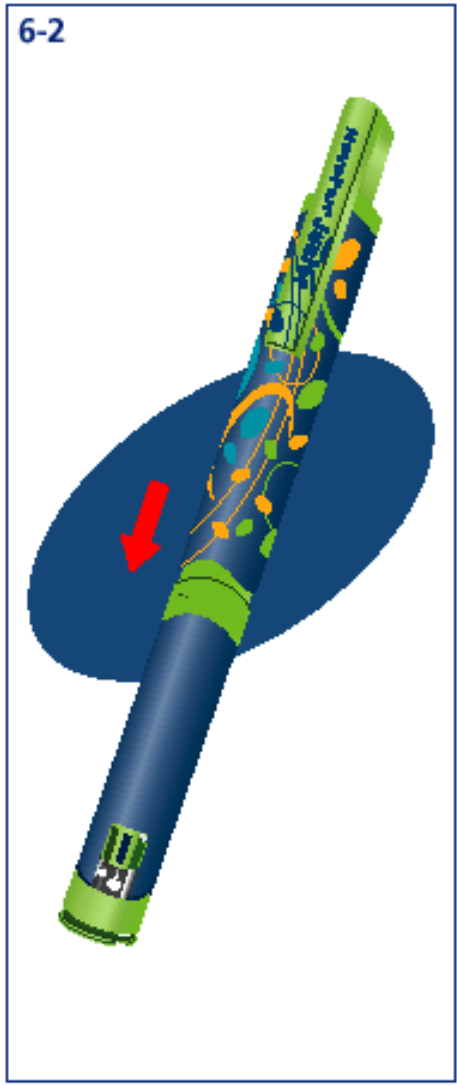
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482 For information on how to throw away needle containers properly, contact your
483 local trash company.
484

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487
488 **SECTION 6 (cont.)**

489
490 **Replace the pen cap:**

- 491
- 492 4. After you remove the disposable needle, hold the pen cap so that the clip
 - 493 is lined up with the dose indicator window.
 - 494
 - 495 5. **Gently slide** the pen cap onto the barrel.
 - 496



Need Help?
Call 1-800-727-6500

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SECTION 7 Removing the PenFill 3 mL Cartridge

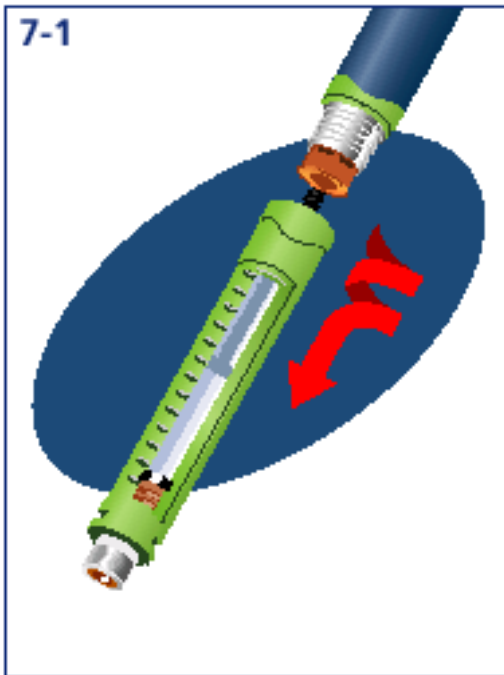
You will need to remove the PenFill cartridge for the following reasons:

- ~~When~~ The PenFill cartridge is empty.
- **If you use a suspension insulin such as Novolin N or Novolin 70/30:**

When you see the rear rubber stopper in the inspection window, then you do not have enough insulin left in the PenFill cartridge for proper mixing.

Remove the barrel:

1. Remove the pen cap.
2. Hold the NovoPen Junior with the dose indicator window at the top.
3. Unscrew the barrel from the cartridge holder.



521
522
523

524 **SECTION 7 (cont.)**

525

526 **Remove the PenFill 3 mL cartridge:**

527

528

4. Tip the cartridge holder. The PenFill cartridge will drop out.

529

530

5. Press the push button all the way in until zero (0) appears in the window.

531

532

6. Turn the end of the reset mechanism in a clockwise direction until the piston rod is no longer sticking out (refer to figure 1-4 on page 7).

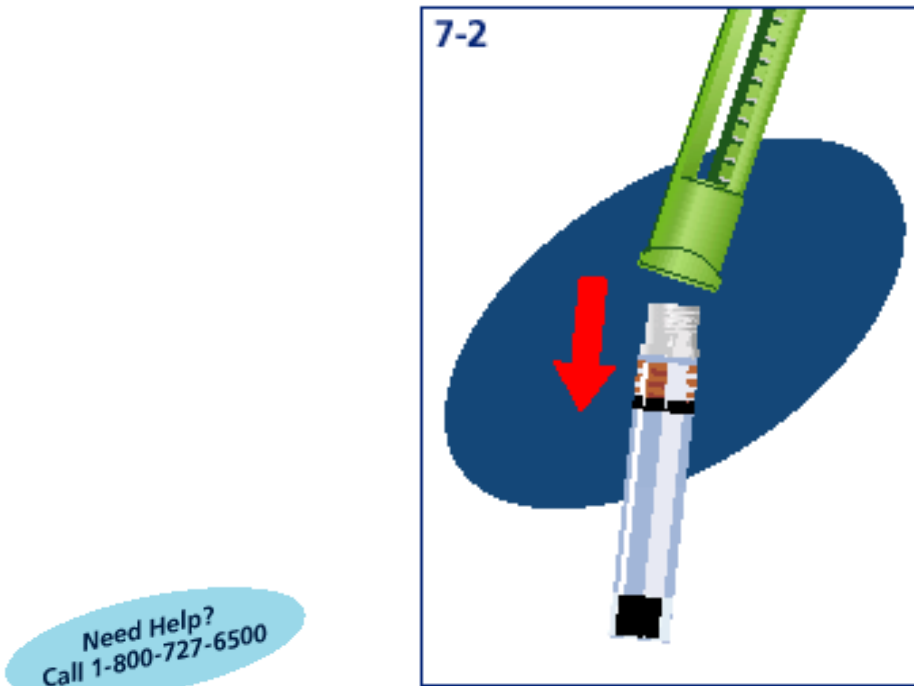
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7. To insert a new PenFill cartridge, please refer to Section 2.

536



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If the reset mechanism locks, it is usually due to improper technique. Gently turn the mechanism side to side until it unlocks and then call our toll free number (1-800-727-6500) so that we may go over your technique with you.

540

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544

FUNCTION CHECK

545

546 You should regularly check the functioning of your NovoPen Junior, (for example,
547 once a month or before starting a new box of PenFill cartridges). The function
548 check is done by delivering 20 units of insulin into the outer needle cap. You will
549 not be injecting insulin into your body.

550

551 Always check the functioning of the NovoPen Junior if you suspect it has been
552 damaged or if you are uncertain that it is delivering the correct dose.

553

554 Do not use NovoPen Junior unless you are sure that it is working properly.

555

556 **To perform the function check:**

557

558 1. Attach a NovoFine disposable needle (see pages 12-15).

559

560 2. Do an air shot (see pages 16-19).

561

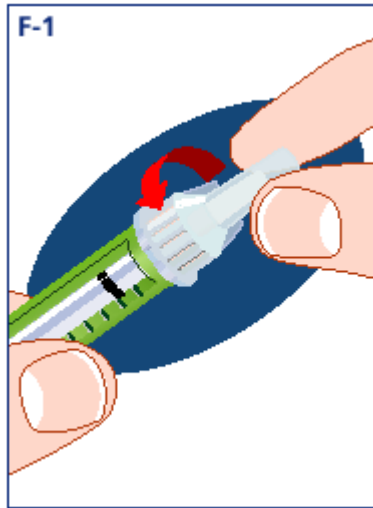
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FUNCTION CHECK (cont.)

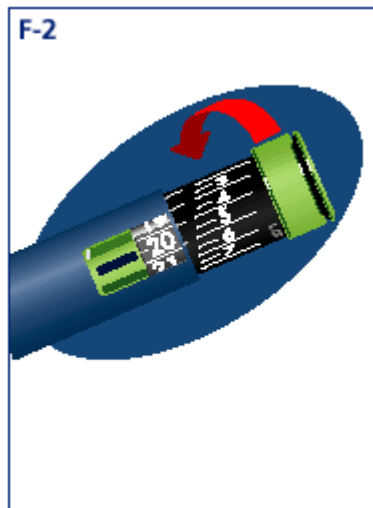
3. **Do not replace the inner needle cap.** Place the outer needle cap securely over the exposed NovoFine needle.



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Expel 20 units of insulin into the outer needle cap:

4. Turn the dial-a-dose selector so the dose indicator window shows 20.



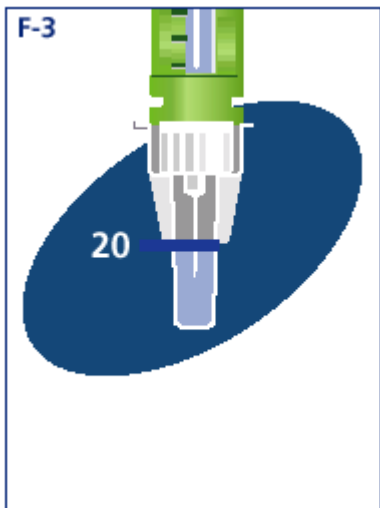
Need Help?
Call 1-800-727-6500

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580 **FUNCTION CHECK (cont.)**

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5. Hold the NovoPen Junior so the NovoFine disposable needle is pointing down.
6. Slowly press the push button **as far as it will go**.
7. Check the dose indicator window to see if it shows zero (0). If it does not show zero (0), there is not enough insulin in the cartridge to do a function check. Insert a new PenFill cartridge (see pages 8-11) and repeat the function check. If there is enough insulin in the cartridge but the dose indicator window does not show zero, repeat the FUNCTION CHECK. If you do not see zero after repeating the above steps, do not use your NovoPen Junior. Contact Novo Nordisk Pharmaceuticals, Inc. at our toll free number (1-800-727-6500).



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The insulin should fill the bottom part of the outer needle cap. This indicates the device is functioning properly.

If the insulin **does not fill or overfills** this part of the cap, review the function check procedure. Then repeat the function check with a new NovoFine disposable needle and outer needle cap.

If the second function check also shows under- or over-filling, do not use your NovoPen Junior.

DO NOT try to repair a NovoPen Junior that you think is not working properly.

612 See Warranty section for further information.

613

614 30

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616

STORAGE

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618

Guidelines for storing the NovoPen Junior and PenFill 3 mL cartridges:

619

620

- PenFill cartridges should be stored in a cool place, such as in a refrigerator, but not in ~~the~~ freezer.

621

622

623

- After the first use of PenFill cartridge in the NovoPen Junior, the NovoPen Junior (with the PenFill cartridge inside) can be kept at room temperature below 86°F (30°C) for the amount of ~~time days specified listed~~ in the PenFill Information for the Patient leaflet for the type of insulin you are using.

624

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- **Do not store** the NovoPen 3 Junior (with the PenFill cartridge inside) in a refrigerator or areas where there may be extreme temperatures or moisture, such as in your car.

630

631

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633

- **The expiration date printed on the cartridge is for unused cartridges under refrigeration. Never use the cartridge after the expiration date on the cartridge or its box.**

634

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- Store the NovoPen Junior **without** the NovoFine needle attached and **with** the pen cap in position.

641

642

643

- For information on storing PenFill cartridges, see the package leaflet that comes in the PenFill cartridge box.

644

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MAINTENANCE

649

650

Guidelines for maintaining the NovoPen Junior.

651

652

Be sure to:

653

654

1. Clean it by wiping with a soft cloth moistened with alcohol.

655

656

2. Protect it from dust, dirt, and moisture when not in its case.

657

658

659

Make certain you:

660

661

1. **Do not** soak it in alcohol, do not wash it in soap and water, or do not lubricate it, since this may cause damage.

662

663

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2. **Do not** expose it to excessive pressure or blows.

665

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3. **Do not** drop it.

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IMPORTANT THINGS TO KNOW

- The NovoPen Junior is not recommended for the blind or visually impaired, without the assistance of a sighted individual trained to use it.
- If you use more than one type of insulin (such as Novolin R, Novolin N, Novolin 70/30, or NovoLog), use a separate insulin delivery device for each type of insulin.
- Use only a new PenFill 3 mL cartridge when loading the NovoPen Junior. Never load the NovoPen Junior with a partially filled PenFill cartridge.
- Always keep a spare insulin delivery system available, in case your NovoPen Junior is lost or damaged.
- Keep the NovoPen Junior, PenFill cartridges, and NovoFine needles out of the reach of children. The American Diabetes Association recommends that insulin should be self-administered. The proper age for initiating this should be assessed by the adult caregiver.
- Keep the NovoPen Junior away from areas where temperatures may get too hot or too cold such as a car or refrigerator.
- The NovoPen Junior is designed for use with PenFill 3 mL insulin cartridges and NovoFine single-use disposable needles.

Novo Nordisk is not responsible for any consequences arising from the use of the NovoPen Junior with products other than PenFill 3 mL insulin cartridges and NovoFine single-use disposable needles.

700 **IMPORTANT NOTES**

701

702 **The following is a review of some important information about the use and**
703 **care of your NovoPen Junior.**

704

705

706 **Before each injection, be certain:**

707

708 1. The NovoPen Junior contains the correct insulin cartridge (such as
709 Novolin R, Novolin N, Novolin 70/30, or NovoLog), if you use more than
710 one type of insulin.

711

712 2. The PenFill cartridge contains enough insulin for mixing, if you use a
713 suspension insulin (white and cloudy) such as Novolin N or Novolin 70/30.

714

715 3. To do an air shot with the NovoFine needle pointing up before each
716 injection.

717

718

719 **Be sure to:**

720

721 1. Check the dose indicator window after each injection to make sure you
722 have received your full dose (see page 23, Section 5).

723

724 2. Remove the NovoFine needle immediately after each injection without
725 replacing the cap.

726

727 3. Select your dose only by using the number in the dose indicator window.

728

729 4. Perform the function check regularly or if you think your NovoPen Junior is
730 not working properly.

731

732 34

733 **IMPORTANT NOTES (cont.)**

734

735 **Make certain you:**

736

737

1. **DO NOT** place a NovoFine needle on the NovoPen Junior until you are ready to do an air shot and give an injection or do a function check. Remove the needle immediately after each injection without replacing the cap. If the NovoFine needle is not removed, some liquid may leak out of the PenFill cartridge. This may cause a change in the strength of suspension insulin (white and cloudy) such as Novolin N or Novolin 70/30.

738

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744

2. **DO NOT** use the clicking sound to set your insulin dose.

745

746

747

3. **DO NOT** try to refill a PenFill cartridge.

748

749

750

751

4. **DO NOT** share the same PenFill cartridge with anyone else even if you attach a new NovoFine needle for each injection. Sharing the cartridge can spread disease. Each PenFill cartridge is for single-person use only.

752

Blood glucose levels should be tested frequently to monitor your insulin regimen.

753

754

Any change in insulin should be made cautiously and only under medical supervision.

755

756

757

758

759 **WHAT TO DO IF...**

760

761 **The dose indicator window does not show zero after the injection:**

762

763 1. **You did not receive your full dose.**

764 Follow the steps on page 23 to get the remaining part of your dose.

765

766 2. **Your NovoPen Junior is malfunctioning.**

767 Do not use your NovoPen Junior. Contact Novo Nordisk Pharmaceuticals,
768 Inc. at our toll free number (1-800-727-6500).

769

770 **No insulin appears when you do the air shot:**

771

772 1. **The piston rod is not far enough down the cartridge holder to reach**
773 **the rear rubber stopper.**

774 Repeat the air shot (see pages 16-19).

775

776 2. **The NovoFine needle may not be securely attached.**

777 a. Put the plastic outer cap back on the NovoFine needle.

778 b. Turn the plastic outer cap in a clockwise direction to tighten the
779 NovoFine needle.

780

781 3. **The NovoFine needle may be blocked.**

782 Change the NovoFine needle (see pages 14-15) and do an air shot (see
783 pages 16-19).

784

785 **The piston rod is sticking out too far to attach the cartridge holder to the**
786 **barrel:**

787

788 You must screw the piston rod back into the barrel (see page 7). Never try to
789 push it in or you can damage the mechanism.

790

791 **The push button will not return to zero or the piston rod will not turn back**
792 **into the reset mechanism:**

793

794 The return mechanism may be locked. This is usually due to improper
795 technique. Gently turn the mechanism side to side until it unlocks and then
796 call our toll free number (1-800-727-6500) so that we may go over your
797 technique with you.

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WARRANTY

Should your NovoPen® Junior device be defective in materials or workmanship within two (2) years of purchase, Novo Nordisk Pharmaceuticals, Inc. will replace it at no charge if you mail the defective unit along with a description of the problem and the sales receipt or other proof of purchase to:

Novo Nordisk Pharmaceuticals, Inc.
Product Safety
100 College Road West
Princeton, NJ 08540

Protected by U.S. Patent Nos. 5,693,027; 5,626,566; 6,126,646 and Des. 347,894 (cartridge) restricted to use with Novo Nordisk insulin cartridges and Novo Nordisk pen needles.

No other warranty is made with respect to NovoPen® Junior. This warranty will be invalid and Novo Nordisk A/S, Novo Nordisk Pharmaceuticals, Inc., Bristol-Myers Squibb Co., Nipro Medical Industries Ltd., and Bang & Olufsen A/S cannot be held responsible in the case of defects or damages arising from:

- The use of the NovoPen® Junior with products other than PenFill 3 mL cartridges and NovoFine single-use disposable needles.
- The use of the NovoPen® Junior not in accordance with the instructions in this booklet.
- Physical damage to the NovoPen® Junior caused by neglect, misuse, unauthorized repair, accident, or other breakage.

For assistance or further information, write to:

Novo Nordisk Pharmaceuticals, Inc.

Customer Relations

100 College Road West

Princeton, NJ 08540

Or call: 1-800-727-6500

NovoPen[®], Novolin[®], NovoLog[®], PenFill[®] and NovoFine[®]
are registered trademarks of Novo Nordisk A/S

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Novo Nordisk Pharmaceuticals, Inc.

Princeton, NJ 08540

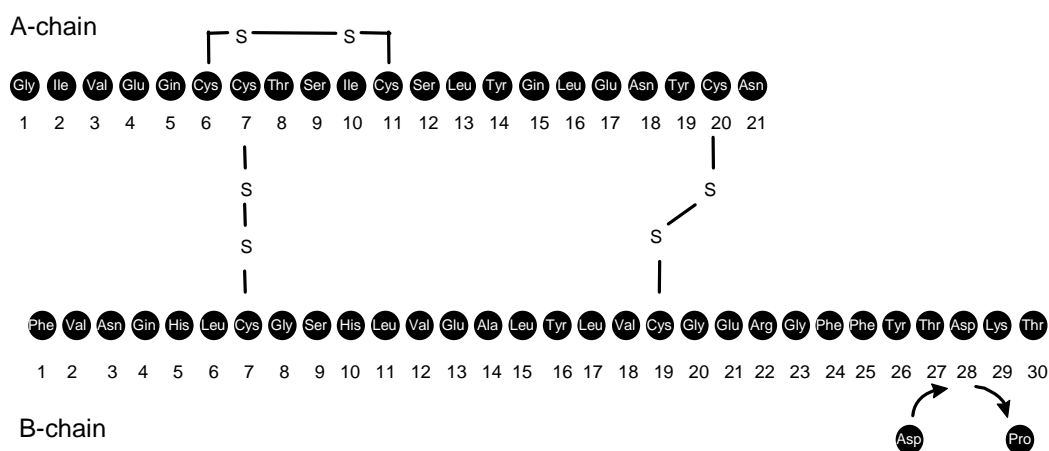
<http://www.novonordisk-us.com>

8-4252-31-003-1

1 **NovoLog[®]**
2 **Insulin aspart (rDNA origin) Injection**

3
4
5 **DESCRIPTION**

6 NovoLog[®] (insulin aspart [rDNA origin] injection) is a human insulin analog that is a rapid-
7 acting, parenteral blood glucose-lowering agent. NovoLog is homologous with regular human
8 insulin with the exception of a single substitution of the amino acid proline by aspartic acid in
9 position B28, and is produced by recombinant DNA technology utilizing *Saccharomyces*
10 *cerevisiae* (baker's yeast) as the production organism. Insulin aspart has the empirical formula
11 C₂₅₆H₃₈₁N₆₅O₇₉S₆ and a molecular weight of 5825.8.



13
14 Figure 1. Structural formula of insulin aspart.

15
16 NovoLog is a sterile, aqueous, clear, and colorless solution, that contains insulin aspart (B28
17 asp regular human insulin analog) 100 Units/mL, glycerin 16 mg/mL, phenol 1.50 mg/mL,
18 metacresol 1.72 mg/mL, zinc 19.6 µg/mL, disodium hydrogen phosphate dihydrate 1.25
19 mg/mL, and sodium chloride 0.58 mg/mL. NovoLog has a pH of 7.2-7.6. Hydrochloric acid
20 10% and/or sodium hydroxide 10% may be added to adjust pH.

21
22 **CLINICAL PHARMACOLOGY**

23 **Mechanism of Action**

24 The primary activity of NovoLog is the regulation of glucose metabolism. Insulins, including
25 NovoLog, bind to the insulin receptors on muscle and fat cells and lower blood glucose by
26 facilitating the cellular uptake of glucose and simultaneously inhibiting the output of glucose
27 from the liver.

28
29 In standard biological assays in mice and rabbits, one unit of NovoLog has the same glucose-
30 lowering effect as one unit of regular human insulin. In humans, the effect of NovoLog is
31 more rapid in onset and of shorter duration, compared to regular human insulin, due to its
32 faster absorption after subcutaneous injection (see Figure 2 and Figure 3).

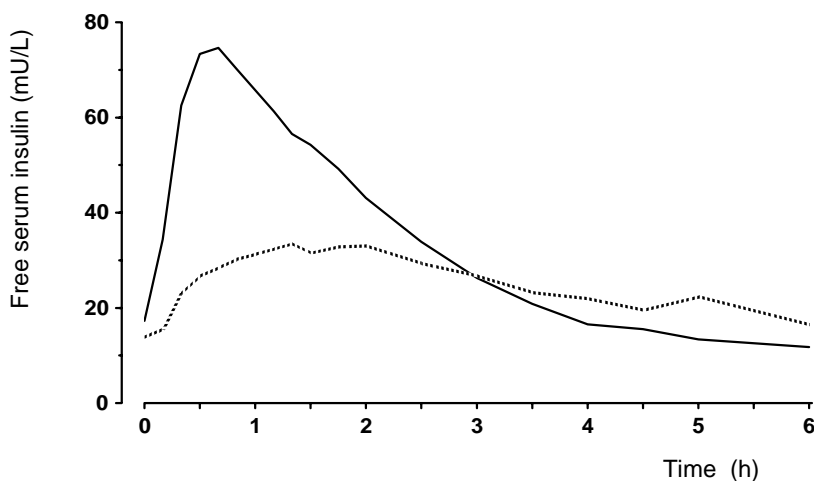
34 **Pharmacokinetics**

35 The single substitution of the amino acid proline with aspartic acid at position B28 in
36 NovoLog reduces the molecule's tendency to form hexamers as observed with regular human
37 insulin. NovoLog is therefore more rapidly absorbed after subcutaneous injection compared to
38 regular human insulin.

39

40 *Bioavailability and Absorption* - NovoLog has a faster absorption, a faster onset of action, and
41 a shorter duration of action than regular human insulin after subcutaneous injection (see Figure
42 2 and Figure 3). The relative bioavailability of NovoLog compared to regular human insulin
43 indicates that the two insulins are absorbed to a similar extent.

44



45

46

47 Figure 2. Serial mean serum free insulin concentration collected up to 6 hours following a
48 single pre-meal dose of NovoLog (solid curve) or regular human insulin (hatched curve)
49 injected immediately before a meal in 22 patients with Type 1 diabetes.

50

51 In studies in healthy volunteers (total n=107) and patients with Type 1 diabetes (total n=40),
52 NovoLog consistently reached peak serum concentrations approximately twice as fast as
53 regular human insulin. The median time to maximum concentration in these trials was 40 to
54 50 minutes for NovoLog versus 80 to 120 minutes for regular human insulin. In a clinical trial
55 in patients with Type 1 diabetes, NovoLog and regular human insulin, both administered
56 subcutaneously at a dose of 0.15 U/kg body weight, reached mean maximum concentrations of
57 82.1 and 35.9 mU/L, respectively. Pharmacokinetic/pharmacodynamic characteristics of
58 insulin aspart have not been established in patients with Type 2 diabetes.

59 The intra-individual variability in time to maximum serum insulin concentration for healthy
60 male volunteers was significantly less for NovoLog than for regular human insulin. The
61 clinical significance of this observation has not been established.

62 In a clinical study in healthy non-obese subjects, the pharmacokinetic differences between
63 NovoLog and regular human insulin described above, were observed independent of the
64 injection site (abdomen, thigh, or upper arm).

65

66 *Distribution and Elimination* - NovoLog has a low binding to plasma proteins, 0-9%, similar
67 to regular human insulin. After subcutaneous administration in normal male volunteers
68 (n=24), NovoLog was more rapidly eliminated than regular human insulin with an average
69 apparent half-life of 81 minutes compared to 141 minutes for regular human insulin.

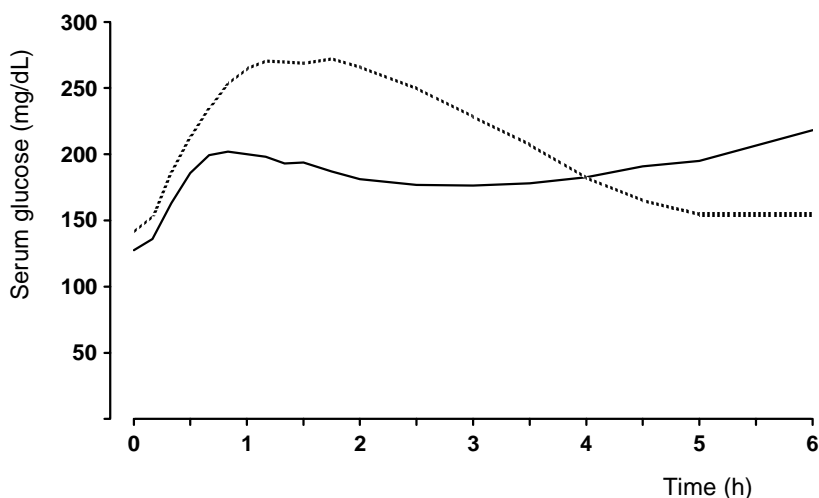
70

71 **Pharmacodynamics**

72 Studies in normal volunteers and patients with diabetes demonstrated that NovoLog has a
73 more rapid onset of action than regular human insulin.

74 In a 6-hour study in patients with Type 1 diabetes (n=22), the maximum glucose-lowering
75 effect of NovoLog occurred between 1 and 3 hours after subcutaneous injection (see Figure 3).
76 The duration of action for NovoLog is 3 to 5 hours compared to 5 to 8 hours for regular human
77 insulin. The time course of action of insulin and insulin analogs such as NovoLog may vary
78 considerably in different individuals or within the same individual. The parameters of
79 NovoLog activity (time of onset, peak time and duration) as designated in Figure 3 should be
80 considered only as general guidelines. The rate of insulin absorption and consequently the
81 onset of activity is known to be affected by the site of injection, exercise, and other variables
82 (see PRECAUTIONS, General).

83



84

85

86 Figure 3. Serial mean serum glucose collected up to 6 hours following a single pre-meal dose
87 of NovoLog (solid curve) or regular human insulin (hatched curve) injected immediately
88 before a meal in 22 patients with Type 1 diabetes.

89

90 **Special Populations**

91 *Children and Adolescents* - The pharmacokinetic and pharmacodynamic properties of
92 NovoLog and regular human insulin were evaluated in a single dose study in 18 children (6-12
93 years, n=9) and adolescents (13-17 years [Tanner grade ≥ 2], n=9) with Type 1 diabetes. The
94 relative differences in pharmacokinetics and pharmacodynamics in children and adolescents
95 with Type 1 diabetes between NovoLog and regular human insulin were similar to those in
96 healthy adult subjects and adults with Type 1 diabetes.

97

98 *Geriatrics* - The effect of age on the pharmacokinetics and pharmacodynamics of NovoLog
99 has not been studied.

100

101 *Gender* - In healthy volunteers, no difference in insulin aspart levels was seen between men
102 and women when body weight differences were taken into account. There was no significant
103 difference in efficacy noted (as assessed by HbA1c) between genders in a trial in patients with
104 Type 1 diabetes.

105

106 *Obesity* - The effect of obesity and/or subcutaneous fat thickness on the pharmacokinetics and
107 glucodynamics of NovoLog has not been studied.

108

109 *Ethnic Origin* - The effect of ethnic origin on the pharmacokinetics of NovoLog has not been
110 studied.

111

112 *Renal Impairment* - Some studies with human insulin have shown increased circulating levels
113 of insulin in patients with renal failure. The effect of renal impairment on the pharmacokinetics
114 of NovoLog has not been studied. Careful glucose monitoring and dose adjustments of
115 insulin, including NovoLog, may be necessary in patients with renal dysfunction (see
116 PRECAUTIONS, Renal Impairment).

117

118 *Hepatic Impairment* - Some studies with human insulin have shown increased circulating
119 levels of insulin in patients with liver failure. The effect of hepatic impairment on the
120 pharmacokinetics of NovoLog has not been studied. Careful glucose monitoring and dose
121 adjustments of insulin, including NovoLog, may be necessary in patients with hepatic
122 dysfunction (see PRECAUTIONS, Hepatic Impairment).

123

124 *Pregnancy* - The effect of pregnancy on the pharmacokinetics and glucodynamics of
125 Novolog has not been studied (see PRECAUTIONS, Pregnancy).

126

127 *Smoking* - The effect of smoking on the pharmacokinetics/pharmacodynamics of NovoLog has
128 not been studied.

129

130 **CLINICAL STUDIES**

131 To evaluate the safety and efficacy of NovoLog in patients with Type 1 diabetes, two
132 six-month, open-label, active-control (NovoLog[®] vs. Novolin[®] R) studies were conducted (see
133 Table 1). NovoLog was administered by subcutaneous injection immediately prior to meals
134 and regular human insulin was administered by subcutaneous injection 30 minutes before
135 meals. NPH insulin was administered as the basal insulin in either single or divided daily
136 doses. Glycemic control (as measured by HbA1c), the rates of hypoglycemia (as determined
137 from the number of events requiring intervention from a third party), and the incidence of
138 ketosis were clinically comparable for the two treatment regimens. The mean total daily doses
139 of insulin were greater (1-3 U/day) in the NovoLog-treated patients compared to patients who
140 received regular human insulin. This difference was primarily due to basal insulin
141 requirements. To achieve the stated levels of glycemic control, some patients required more

142 than three doses of meal-related insulin and/or more than one dose of basal insulin (see Table
 143 1). No serum glucose measurements were obtained in these studies.

144
 145 To evaluate the safety and efficacy of NovoLog in patients with Type 2 diabetes, one six-
 146 month, open-label, active-control (NovoLog[®] vs. Novolin[®] R) study was conducted (see Table
 147 1). NovoLog was administered by subcutaneous injection immediately prior to meals and
 148 regular human insulin was administered by subcutaneous injection 30 minutes before meals.
 149 NPH insulin was administered as the basal insulin in either single or divided daily doses.
 150 Glycemic control (as measured by HbA1c) and the rates of hypoglycemia (as determined from
 151 the number of events requiring intervention from a third party) were clinically comparable for
 152 the two treatment regimens. The mean total daily dose of insulin was greater (2 U/day) in the
 153 NovoLog-treated patients compared to patients who received regular human insulin. This
 154 difference was primarily due to basal insulin requirements. To achieve the stated levels of
 155 glycemic control, some patients required more than three doses of meal-related insulin and/or
 156 more than one dose of basal insulin (see Table 1).

157
 158 Table 1. Results of two six-month, active-control, open-label trials in patients with Type 1
 159 diabetes (Studies A and B) and one six-month, active-control, open-label trial in patients with
 160 Type 2 diabetes (Study C).

161

Study	Treatment (n)	Mean HbA1c (%)		Hypoglycemia ¹ (events / month / patient)	% of Patients Using Various Numbers of Insulin Injections / Day ²				
		Baseline	Month 6		Rapid-acting			Basal	
					1 - 2	3	4 - 5	1	2
A	NovoLog (n=694)	8.0	7.9	0.06	3	75	22	54	46
	Novolin R (n=346)	8.0	8.0	0.06	6	75	19	63	37
B	NovoLog (n=573)	7.9	7.8	0.08	4	90	6	94	6
	Novolin R (n=272)	8.0	7.9	0.06	4	91	4	93	7
C	NovoLog (n=90)	8.1	7.7	0.02	4	93	4	97	4
	Novolin R (n=86)	7.8	7.8	0.01	2	93	5	93	7

162 ¹ Events requiring intervention from a third party during the last three months of treatment

163 ² Percentages are rounded to the nearest whole number

164

165 To evaluate the use of NovoLog by subcutaneous infusion with an external pump, two open-
 166 label, parallel design studies (6 weeks [n=29] and 16 weeks [n=118]) compared NovoLog
 167 versus Velosulin (buffered regular human insulin) in patients with Type 1 diabetes. Glycemic
 168 control (as measured by HbA1c) and rates of hypoglycemia were comparable. Patients with
 169 Type 2 diabetes were also studied in an open-label, parallel design trial (16 weeks [n=127])
 170 using NovoLog by subcutaneous infusion compared to pre-prandial injection (in conjunction
 171 with basal NPH injections). Reductions in HbA1c and rates of hypoglycemia were comparable.
 172 (See INDICATIONS AND USAGE, WARNINGS, PRECAUTIONS, Mixing of Insulins,
 173 Information for Patients, DOSAGE AND ADMINISTRATION, and RECOMMENDED
 174 STORAGE.)

175

176 **INDICATIONS AND USAGE**

177 NovoLog is indicated for the treatment of adult patients with diabetes mellitus, for the control
178 of hyperglycemia. Because NovoLog has a more rapid onset and a shorter duration of activity
179 than human regular insulin, NovoLog given by injection should normally be used in regimens
180 with an intermediate or long-acting insulin. NovoLog may also be infused subcutaneously by
181 external insulin pumps. (See WARNINGS, PRECAUTIONS [especially Usage in Pumps],
182 Information for Patients [especially For Patients Using Pumps], Mixing of Insulins, DOSAGE
183 AND ADMINISTRATION, RECOMMENDED STORAGE.)

184 **CONTRAINDICATIONS**

185 NovoLog is contraindicated during episodes of hypoglycemia and in patients hypersensitive to
186 NovoLog or one of its excipients.

188 **WARNINGS**

189 **NovoLog differs from regular human insulin by a more rapid onset and a shorter**
190 **duration of activity. Because of the fast onset of action, the injection of NovoLog should**
191 **immediately be followed by a meal. Because of the short duration of action of NovoLog,**
192 **patients with diabetes also require a longer-acting insulin to maintain adequate glucose**
193 **control. Glucose monitoring is recommended for all patients with diabetes and is**
194 **particularly important for patients using external pump infusion therapy.**

195
196
197 **Hypoglycemia is the most common adverse effect of insulin therapy, including NovoLog.**
198 **As with all insulins, the timing of hypoglycemia may differ among various insulin**
199 **formulations.**

200
201 **Any change of insulin dose should be made cautiously and only under medical**
202 **supervision. Changes in insulin strength, manufacturer, type (e.g., regular, NPH,**
203 **analog), species (animal, human), or method of manufacture (rDNA versus animal-**
204 **source insulin) may result in the need for a change in dosage.**

205
206 **Insulin Pumps: When used in an external insulin pump for subcutaneous infusion,**
207 **NovoLog should not be diluted or mixed with any other insulin. Physicians and patients**
208 **should carefully evaluate information on pump use in the NovoLog physician and patient**
209 **package inserts and in the pump manufacturer's manual (e.g. NovoLog-specific**
210 **information should be followed for in-use time, frequency of changing infusion sets, or**
211 **other details specific to NovoLog usage, because NovoLog-specific information may**
212 **differ from general pump manual instructions). Pump or infusion set malfunctions or**
213 **insulin degradation can lead to hyperglycemia and ketosis in a short time because of the**
214 **small subcutaneous depot of insulin. This is especially pertinent for rapid-acting insulin**
215 **analogs that are more rapidly absorbed through skin and have shorter duration of**
216 **action. These differences may be particularly relevant when patients are switched from**
217 **multiple injection therapy or infusion with buffered regular insulin. Prompt**
218 **identification and correction of the cause of hyperglycemia or ketosis is necessary.**
219 **Interim therapy with subcutaneous injection may be required. (See PRECAUTIONS,**

220 **Mixing of Insulins, Information for Patients, DOSAGE AND ADMINISTRATION, and**
221 **RECOMMENDED STORAGE.)**

222

223 **PRECAUTIONS**

224 **General**

225 Hypoglycemia and hypokalemia are among the potential clinical adverse effects associated
226 with the use of all insulins. Because of differences in the action of NovoLog and other
227 insulins, care should be taken in patients in whom such potential side effects might be
228 clinically relevant (e.g., patients who are fasting, have autonomic neuropathy, or are using
229 potassium-lowering drugs or patients taking drugs sensitive to serum potassium level).

230 Lipodystrophy and hypersensitivity are among other potential clinical adverse effects
231 associated with the use of all insulins.

232 As with all insulin preparations, the time course of NovoLog action may vary in different
233 individuals or at different times in the same individual and is dependent on site of injection,
234 blood supply, temperature, and physical activity.

235 Adjustment of dosage of any insulin may be necessary if patients change their physical activity
236 or their usual meal plan. Insulin requirements may be altered during illness, emotional
237 disturbances, or other stresses.

238

239 *Hypoglycemia* - As with all insulin preparations, hypoglycemic reactions may be associated
240 with the administration of NovoLog. Rapid changes in serum glucose levels may induce
241 symptoms of hypoglycemia in persons with diabetes, regardless of the glucose value. Early
242 warning symptoms of hypoglycemia may be different or less pronounced under certain
243 conditions, such as long duration of diabetes, diabetic nerve disease, use of medications such
244 as beta-blockers, or intensified diabetes control (see PRECAUTIONS, Drug Interactions).
245 Such situations may result in severe hypoglycemia (and, possibly, loss of consciousness) prior
246 to patients' awareness of hypoglycemia.

247

248 *Renal Impairment* - Although there are no specific data in patients with diabetes and renal
249 impairment treated with NovoLog, NovoLog dose requirements may be reduced in the
250 presence of renal impairment, similar to observations with other insulins (see CLINICAL
251 PHARMACOLOGY, Pharmacokinetics).

252

253 *Hepatic Impairment* - Although there are no specific data in patients with diabetes and
254 hepatic disease treated with NovoLog, NovoLog dose requirements may be reduced in the
255 presence of impaired hepatic function, similar to observations found with other insulins (see
256 CLINICAL PHARMACOLOGY, Pharmacokinetics).

257

258 *Allergy - Local Allergy* - As with other insulin therapy, patients may experience redness,
259 swelling, or itching at the site of injection. These minor reactions usually resolve in a few days
260 to a few weeks, but in some occasions, may require discontinuation of NovoLog. In some
261 instances, these reactions may be related to factors other than insulin, such as irritants in a skin
262 cleansing agent or poor injection technique.

263 *Systemic Allergy* - Less common, but potentially more serious, is generalized allergy to insulin,
264 which may cause rash (including pruritus) over the whole body, shortness of breath, wheezing,

265 reduction in blood pressure, rapid pulse, or sweating. Severe cases of generalized allergy,
266 including anaphylactic reaction, may be life threatening.

267 Localized reactions and generalized myalgias have been reported with the use of cresol as an
268 injectable excipient.

269 In controlled clinical trials using injection therapy, allergic reactions were reported in 3 of 735
270 patients (0.4%) who received regular human insulin and 10 of 1394 patients (0.7%) who
271 received NovoLog. During these and other trials, 3 of 2341 patients treated with NovoLog
272 were discontinued due to allergic reactions.

273

274 *Antibody Production* - Insulin antibodies may develop during treatment with insulin. In large
275 clinical trials, levels of antibodies that cross react with human insulin and insulin aspart were
276 higher in patients treated with NovoLog compared to regular human insulin. The clinical
277 significance of these antibodies is uncertain.

278

279 *Pregnancy and Lactation*

280 Female patients should be advised to tell their physician if they intend to become, or if they
281 become pregnant. Information is not available on the use of NovoLog during pregnancy or
282 lactation.

283

284 *Usage in Pumps*

285 NovoLog is recommended for use in Disetronic H-TRON[®] plus V100 with Disetronic 3.15
286 plastic cartridges and Classic or Tender infusion sets; MiniMed Models 505, 506, or 507 with
287 MiniMed 3 mL syringes and Polyfin[®] or Sof-set[®] infusion sets.

288

289 In-vitro studies have shown that pump malfunction, loss of cresol, and insulin degradation,
290 may occur with the use of NovoLog for more than two days at 37°C (98.6°F) in infusion sets
291 and reservoirs. NovoLog in clinical use should not be exposed to temperatures greater than
292 37°C (98.6°F). **NovoLog should not be mixed with other insulins or with a diluent when it
293 is used in the pump.** (See WARNINGS, PRECAUTIONS, Mixing of Insulins, Information
294 for Patients, DOSAGE AND ADMINISTRATION, and RECOMMENDED STORAGE.)

295

296

297 **Information for Patients**

298

299 *For all patients:*

300 Patients should be informed about potential risks and advantages of NovoLog therapy
301 including the possible side effects. Patients should also be offered continued education and
302 advice on insulin therapies, injection technique, life-style management, regular glucose
303 monitoring, periodic glycosylated hemoglobin testing, recognition and management of hypo-
304 and hyperglycemia, adherence to meal planning, complications of insulin therapy, timing of
305 dose, instruction in the use of injection or subcutaneous infusion devices, and proper storage of
306 insulin. Patients should be informed that frequent, patient-performed blood glucose
307 measurements are needed to achieve optimal glycemic control and avoid both hyper- and
308 hypoglycemia.

309

310 Female patients should be advised to tell their physician if they intend to become, or if they
311 become pregnant. Information is not available on the use of NovoLog during pregnancy or
312 lactation (see PRECAUTIONS, Pregnancy).

313

314 ***For patients using pumps***

315 Patients using external pump infusion therapy should be trained in intensive insulin therapy
316 with multiple injections and in the function of their pump and pump accessories. NovoLog is
317 recommended for use with Disetronic H-TRON plus V100 with Disetronic 3.15 plastic
318 cartridges and Classic or Tender infusion sets; MiniMed Models 505, 506, and 507 with
319 MiniMed 3 mL syringes and Polyfin or Sof-set infusion sets. The use of NovoLog in quick-
320 release infusion sets and cartridge adapters has not been assessed.

321

322 **To avoid insulin degradation, infusion set occlusion, and loss of the preservative (cresol),**
323 **the infusion sets (reservoir syringe, tubing, and catheter) and the NovoLog in the**
324 **reservoir should be replaced, and a new infusion site selected every 48 hours or less.**

325 **Insulin exposed to temperatures higher than 37°C (98.6°F) should be discarded.** The
326 temperature of the insulin may exceed ambient temperature when the pump housing, cover,
327 tubing, or sport case is exposed to sunlight or radiant heat. Infusion sites that are erythematous,
328 pruritic, or thickened should be reported to medical personnel, and a new site selected because
329 continued infusion may increase the skin reaction and/or alter the absorption of NovoLog.

330

331 Pump or infusion set malfunctions or insulin degradation can lead to hyperglycemia and
332 ketosis in a short time because of the small subcutaneous depot of insulin. This is especially
333 pertinent for rapid-acting insulin analogs that are more rapidly absorbed through skin and have
334 shorter duration of action. These differences are particularly relevant when patients are
335 switched from infused buffered regular insulin or multiple injection therapy. Prompt
336 identification and correction of the cause of hyperglycemia or ketosis is necessary. Problems
337 include pump malfunction, infusion set occlusion, leakage, disconnection or kinking, and
338 degraded insulin. Less commonly, hypoglycemia from pump malfunction may occur. If these
339 problems cannot be promptly corrected, patients should resume therapy with subcutaneous
340 insulin injection and contact their physician. (See WARNINGS, PRECAUTIONS, Mixing of
341 Insulins, DOSAGE AND ADMINISTRATION, and RECOMMENDED STORAGE.)

342

343 **Laboratory Tests**

344 As with all insulin therapy, the therapeutic response to NovoLog should be monitored by
345 periodic blood glucose tests. Periodic measurement of glycosylated hemoglobin is
346 recommended for the monitoring of long-term glycemic control.

347

348 **Drug Interactions**

349 A number of substances affect glucose metabolism and may require insulin dose adjustment
350 and particularly close monitoring.

- 351 • The following are examples of substances that may increase the blood-glucose-lowering
352 effect and susceptibility to hypoglycemia: oral antidiabetic products, ACE inhibitors,
353 disopyramide, fibrates, fluoxetine, monoamine oxidase (MAO) inhibitors, propoxyphene,
354 salicylates, somatostatin analog (e.g., octreotide), sulfonamide antibiotics.

- 355 • The following are examples of substances that may reduce the blood-glucose-lowering
356 effect: corticosteroids, niacin, danazol, diuretics, sympathomimetic agents (e.g.,
357 epinephrine, salbutamol, terbutaline), isoniazid, phenothiazine derivatives, somatropin,
358 thyroid hormones, estrogens, progestogens (e.g., in oral contraceptives).
- 359 • Beta-blockers, clonidine, lithium salts, and alcohol may either potentiate or weaken the
360 blood-glucose-lowering effect of insulin. Pentamidine may cause hypoglycemia, which
361 may sometimes be followed by hyperglycemia.
- 362 • In addition, under the influence of sympatholytic medicinal products such as beta-blockers,
363 clonidine, guanethidine, and reserpine, the signs of hypoglycemia may be reduced or
364 absent (see CLINICAL PHARMACOLOGY).
- 365

366 **Mixing of Insulins**

- 367 • A clinical study in healthy male volunteers (n=24) demonstrated that mixing NovoLog
368 with NPH human insulin immediately before injection produced some attenuation in the
369 peak concentration of NovoLog, but that the time to peak and the total bioavailability of
370 NovoLog were not significantly affected. If NovoLog is mixed with NPH human insulin,
371 NovoLog should be drawn into the syringe first. The injection should be made
372 immediately after mixing. Because there are no data on the compatibility of NovoLog and
373 crystalline zinc insulin preparations, NovoLog should not be mixed with these
374 preparations.
- 375 • The effects of mixing NovoLog with insulins of animal source or insulin preparations
376 produced by other manufacturers have not been studied (see WARNINGS).
- 377 • Mixtures should not be administered intravenously.
- 378 • When used in external subcutaneous infusion pumps for insulin, NovoLog should not be
379 mixed with any other insulins or diluent.
- 380

381 **Carcinogenicity, Mutagenicity, Impairment of Fertility**

382 Standard 2-year carcinogenicity studies in animals have not been performed to evaluate the
383 carcinogenic potential of NovoLog. In 52-week studies, Sprague-Dawley rats were dosed
384 subcutaneously with NovoLog at 10, 50, and 200 U/kg/day (approximately 2, 8, and 32 times
385 the human subcutaneous dose of 1.0 U/kg/day, based on U/body surface area, respectively). At
386 a dose of 200 U/kg/day, NovoLog increased the incidence of mammary gland tumors in
387 females when compared to untreated controls. The incidence of mammary tumors for
388 NovoLog was not significantly different than for regular human insulin. The relevance of
389 these findings to humans is not known. NovoLog was not genotoxic in the following tests:
390 Ames test, mouse lymphoma cell forward gene mutation test, human peripheral blood
391 lymphocyte chromosome aberration test, in vivo micronucleus test in mice, and in *ex vivo*
392 UDS test in rat liver hepatocytes. In fertility studies in male and female rats, at subcutaneous
393 doses up to 200 U/kg/day (approximately 32 times the human subcutaneous dose, based on
394 U/body surface area), no direct adverse effects on male and female fertility, or general
395 reproductive performance of animals was observed.

396

397 **Pregnancy - Teratogenic Effects - Pregnancy Category C**

398 There are no adequate well-controlled clinical studies of the use of NovoLog in pregnant
399 women. NovoLog should be used during pregnancy only if the potential benefit justifies the
400 potential risk to the fetus.

401

402 It is essential for patients with diabetes or history of gestational diabetes to maintain good
403 metabolic control before conception and throughout pregnancy. Insulin requirements may
404 decrease during the first trimester, generally increase during the second and third trimesters,
405 and rapidly decline after delivery. Careful monitoring of glucose control is essential in such
406 patients.

407

408 Subcutaneous reproduction and teratology studies have been performed with NovoLog and
409 regular human insulin in rats and rabbits. In these studies, NovoLog was given to female rats
410 before mating, during mating, and throughout pregnancy, and to rabbits during organogenesis.
411 The effects of NovoLog did not differ from those observed with subcutaneous regular human
412 insulin. NovoLog, like human insulin, caused pre- and post-implantation losses and
413 visceral/skeletal abnormalities in rats at a dose of 200 U/kg/day (approximately 32 times the
414 human subcutaneous dose of 1.0 U/kg/day, based on U/body surface area) and in rabbits at a
415 dose of 10 U/kg/day (approximately three times the human subcutaneous dose of 1.0 U/kg/day,
416 based on U/body surface area). The effects are probably secondary to maternal hypoglycemia
417 at high doses. No significant effects were observed in rats at a dose of 50 U/kg/day and rabbits
418 at a dose of 3 U/kg/day. These doses are approximately 8 times the human subcutaneous dose
419 of 1.0 U/kg/day for rats and equal to the human subcutaneous dose of 1.0 U/kg/day for rabbits,
420 based on U/body surface area.

421

422 **Nursing Mothers**

423 It is unknown whether insulin aspart is excreted in human milk. Many drugs, including human
424 insulin, are excreted in human milk. For this reason, caution should be exercised when
425 NovoLog is administered to a nursing mother.

426

427 **Pediatric Use**

428 Safety and effectiveness of NovoLog in children have not been studied.

429

430 **Geriatric Use**

431 In the large controlled clinical trials, 36 patients \geq 65 years of age were treated with NovoLog.
432 No conclusions regarding the safety and efficacy of NovoLog in the elderly patients compared
433 to younger adults can be reached from this limited data set.

434

435 **ADVERSE REACTIONS**

436 Clinical trials comparing NovoLog with regular human insulin did not demonstrate a
437 difference in frequency of adverse events between the two treatments.

438 Adverse events commonly associated with human insulin therapy include the following:

439 **Body as Whole** - *Allergic reactions* (see PRECAUTIONS, Allergy).

440 **Skin and Appendages** - *Injection site reaction, lipodystrophy, pruritus, rash* (see
441 PRECAUTIONS, Allergy; Information for Patients, Usage in Pumps.).

442 **Other** – *Hypoglycemia, Hyperglycemia and ketosis* (see WARNINGS and PRECAUTIONS).

443 In controlled clinical trials, small, but persistent elevations in alkaline phosphatase result were
444 observed in some patients treated with NovoLog. The clinical significance of this finding is
445 unknown.

446

447 **OVERDOSAGE**

448 Hypoglycemia may occur as a result of an excess of insulin relative to food intake, energy
449 expenditure, or both. Mild episodes of hypoglycemia usually can be treated with oral glucose.
450 Adjustments in drug dosage, meal patterns, or exercise, may be needed. More severe episodes
451 with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous
452 glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation
453 may be necessary because hypoglycemia may recur after apparent clinical recovery.

454

455 **DOSAGE AND ADMINISTRATION**

456 NovoLog should generally be given immediately before a meal (start of meal within 5-10
457 minutes after injection) because of its fast onset of action. The dosage of
458 NovoLog should be individualized and determined, based on the physician's advice, in
459 accordance with the needs of the patient. The total daily individual insulin requirement is
460 usually between 0.5-1.0 units/kg/day. When used in a meal-related subcutaneous injection
461 treatment regimen, 50-70% of total insulin requirements may be provided by NovoLog and the
462 remainder provided by an intermediate-acting or long-acting insulin. When used in external
463 insulin infusion pumps, the initial programming of the pump is based on the total daily insulin
464 dose of the previous regimen. Although there is significant interpatient variability,
465 approximately 50% of the total dose is given as meal-related boluses of NovoLog and the
466 remainder as basal infusion. Because of NovoLog's comparatively rapid onset and short
467 duration of glucose lowering activity, some patients may require more basal insulin and more
468 total insulin to prevent pre-meal hyperglycemia when using NovoLog than when using human
469 regular insulin. Additional basal insulin injections, or higher basal rates in external
470 subcutaneous infusion pumps may be necessary. **Infusion sets and the insulin in the infusion
471 sets must be changed every 48 hours or sooner to assure the activity of NovoLog and
472 proper pump function.** (See WARNINGS, PRECAUTIONS, Information for Patients)

473

474 NovoLog should be administered by subcutaneous injection in the abdominal wall, the thigh,
475 or the upper arm, or by continuous subcutaneous infusion in the abdominal wall. Injection
476 sites and infusion sites should be rotated within the same region. As with all insulins, the
477 duration of action will vary according to the dose, injection site, blood flow, temperature, and
478 level of physical activity.

479 Parenteral drug products should be inspected visually for particulate matter and discoloration
480 prior to administration, whenever solution and container permit. Never use any NovoLog if it
481 has become viscous (thickened) or cloudy; use it only if it is clear and colorless. NovoLog
482 should not be used after the printed expiration date.

483

484 **HOW SUPPLIED**

485 NovoLog[®] is available in the following package sizes: each presentation containing 100 Units
486 of insulin aspart per mL (U-100).

487 10 mL vials

NDC 0169-7501-11

488 3 mL PenFill[®] cartridges* NDC 0169-3303-12
489

490 * NovoLog[®] PenFill[®] cartridges are for use with NovoPen[®]3, NovoPen[®]3 Demi, and NovoPen
491 Junior Insulin Delivery Devices
492 and NovoFine[®] disposable needles.
493

494 **RECOMMENDED STORAGE**

495 NovoLog in unopened vials and cartridges should be stored between 2° and 8°C (36° to 46°F).
496 *Do not freeze. Do not use NovoLog if it has been frozen or exposed to temperatures that*
497 **exceed 37°C (98.6°F).** After a vial or cartridge has been punctured, it may be kept at
498 temperatures below 30°C (86°F) for up to 28 days, but should not be exposed to excessive heat
499 or sunlight. Opened vials may be refrigerated. Cartridges should not be refrigerated after
500 insertion into the NovoPen 3. Infusion sets (reservoirs, tubing, and catheters) and the NovoLog
501 in the reservoir should be discarded after no more than 48 hours of use or after exposure to
502 temperatures that exceed 37°C (98.6°F).
503

504 Rx only
505

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507 8-XXXX-XX-XXX-X
508

509 Manufactured For Novo Nordisk Pharmaceuticals Inc., Princeton, New Jersey 08540
510 www.novonordisk-us.com

511 Manufactured By Novo Nordisk A/S, 2880 Bagsvaerd, Denmark
512

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516 H-TRON[®] is a trademark of Disetronic Medical Systems, Inc.

1
2
3 **Information For The Patient**
4 **NovoLog[®] (Insulin aspart [rDNA origin] Injection)**
5 **3 mL PenFill[®] Disposable Cartridge (300 units per cartridge)**
6 **10 mL Vial (1000 units per vial)**
7 **100 units/mL (U-100)**

- 8 • What is the most important information I should know about NovoLog?
9 • For all NovoLog users
10 • For pump users
11 • What is NovoLog?
12 • Who should not use NovoLog?
13 • What should I know about using insulin?
14 • What should I know about using NovoLog?
15 • What should I avoid when using NovoLog?
16 • What are the possible side effects of NovoLog?
17 • How should I store NovoLog?
18 • General advice
19 • Injection and pump infusion instructions
20 • How should I inject NovoLog?
21 • Using Vials
22 • Using Cartridges
23 • How should I infuse NovoLog with an external subcutaneous insulin infusion
24 pump?
25 • How should I mix insulins?

26
27 Read this information carefully before you begin treatment. Read the information you
28 get whenever you get more medicine. There may be new information. This information
29 does not take the place of talking with your doctor about your medical condition or your
30 treatment. If you have any questions about NovoLog[®] (NO-voe-log), ask your doctor.
31 Only your doctor can determine if NovoLog[®] is right for you.

32
33 **What is the most important information I should know about NovoLog?**

34
35 *For All NovoLog Users*

- 36 • NovoLog (NO-voe-log) is different from regular human insulin and buffered regular
37 human insulin (Velosulin). It works faster (rapid onset of action) and will not work as
38 long (shorter duration of action) as regular human insulin or buffered regular human
39 insulin (Velosulin).
40
41 • Because the onset of action is fast, you should eat a meal 5-10 minutes after a
42 NovoLog injection or NovoLog bolus infusion dose given by an external pump. (A
43 bolus is a large dose.) Eating right after the dose will reduce the risk of low blood
44 sugar (hypoglycemia).
45

- 46 • The shorter duration of NovoLog's action means that you may need to use an
47 intermediate or longer-acting insulin (basal insulin) or higher basal rates of NovoLog
48 insulin infusion in the pump. This will give the best glucose control and will help you
49 avoid hyperglycemia (high blood sugar) and ketoacidosis (too much acid [low pH] in
50 your body).
- 51
- 52 • Glucose monitoring is recommended for all patients who use insulin.

53

54 If you use NovoLog by injection, you may need to increase some or all of the following:

55

- your total dose of insulin
- your dose of intermediate or long-acting insulin (for example, NPH)
- the number of injections of basal insulin

56

57

58

59 If you infuse NovoLog into the skin (subcutaneous tissue) by pump, you may need to
60 increase some or all of the following:

61

- your total insulin dose
- the basal infusion dose
- the proportion of total insulin given as a basal infusion

62

63

64

65 Age and exposure to heat affect the stability of NovoLog and its preservative. Also,
66 NovoLog does not work well after it has been frozen. Therefore, do not use old insulin or
67 insulin that has been exposed to temperature extremes. Hyperglycemia may be a sign that
68 the insulin is no longer working and needs to be replaced.

69

70

Do not mix NovoLog:

71

- with any other insulins when used in a pump
- with Lantus[®] (insulin glargine [rDNA origin] injection) when used with injections
by syringe

72

(You may, however, mix NovoLog with NPH when used with injections by syringe.
See: How should I mix insulins?)

73

74

75

76

For Pump Users

77

78 • Glucose monitoring is very important for patients using external pump subcutaneous
79 infusion therapy. You should be aware that pump or infusion set malfunctions that
80 result in inadequate insulin infusion can quickly lead to hyperglycemia and ketosis.
81 Accordingly, problems with the infusion pump, the flow of insulin, or the quality of
82 the insulin should be identified and corrected as quickly as possible. There is only a
83 small amount of insulin infused into the skin with a pump. The faster absorption
84 through the skin of rapid-acting insulin analogs and shorter duration of action may
85 give you less time to identify and correct the problem than with buffered regular
86 insulin.

87

88

89 • Therefore, you should dose with insulin from a new vial of NovoLog if unexplained
hyperglycemia or pump alarms do not respond to all of the following:

90

- a repeat dose (injection or bolus) of NovoLog

- 91 • a change in the infusion set, including the NovoLog in the reservoir
- 92 • a change in the infusion site

93

94 If these measures do not work, you may need to resume skin (subcutaneous)
95 injections with syringes or insulin pens. Continue to monitor your glucose and
96 ketones. If problems continue, you must contact your doctor.

97

- 98 • When NovoLog is used in an external subcutaneous insulin infusion pump, you
99 should use only recommended pumps and infusion sets (insulin reservoirs, tubing,
100 catheters). The infusion set, reservoir insulin, and infusion site should be changed:
101 • at intervals of 48 hours or less
102 • with unexpected hyperglycemia or ketosis
103 • when alarms sound, as specified by your MiniMed or Disetronic pump manual
104 • if the insulin or pump has been exposed to temperatures over 98.6°F (37°C), as it
105 might be in a sauna, with long showers, or on a hot day
106 • if the insulin or pump could have absorbed radiant heat, for example from
107 sunlight, that would heat the insulin to over 98.6°F (37°C). Dark colored pump
108 cases or sport covers can increase this type of heat. The location where the pump
109 is worn may also affect the temperature

110

111 Patients who develop “pump bumps” (skin reactions at the infusion site) may need to
112 change infusion sites more often.

113

114 **For your safety, read the section “What are the possible side effects of NovoLog?” to**
115 **review the symptoms of low blood sugar (hypoglycemia) and high blood sugar**
116 **(hyperglycemia).**

117

118 **What is NovoLog?**

119 NovoLog is a clear, colorless, sterile solution for injection or infusion under the skin
120 (subcutaneously). NovoLog is a human-made form of insulin to lower your blood sugar
121 faster than human regular insulin. Because the insulin is human-made by recombinant
122 DNA technology (rDNA) and is chemically different from the insulin made by the human
123 body, it is called an insulin analog. The active ingredient in NovoLog is insulin aspart.
124 The concentration of insulin aspart is 100 units per milliliter, or U100. NovoLog also
125 contains: glycerin, phenol, metacresol, zinc, disodium hydrogen phosphate dihydrate,
126 and sodium chloride. Hydrochloric acid and/or sodium hydroxide may be added to adjust
127 the pH. These ingredients help to preserve or stabilize NovoLog insulin. The pH
128 (balance between acid and alkaline conditions) is important to the stability of NovoLog.
129 Increases in temperature can affect the stability of NovoLog, so it may not work well.

130

131 **Who should not use NovoLog?**

132 Do not use NovoLog if:

- 133 • your blood sugar (glucose) is too low (hypoglycemia)
- 134 • you do not plan to eat right after your injection or infusion

- 135 • you are allergic to insulin aspart or any of the ingredients contained in NovoLog
136 (check with your doctor if you are not sure)

137

138 The effects of NovoLog on an unborn child or on a nursing baby are unknown.
139 Therefore, tell your doctor if you plan to become pregnant or breast feed, or if you
140 become pregnant. You may need to use another medicine.

141

142 Tell your doctor about all medicines and supplements that you are using. Some
143 medicines, including non-prescription medicines and dietary supplements, may affect
144 your diabetes.

145

146 **What should I know about using insulin?**

- 147 • Make any change of insulin cautiously and only under medical supervision. Changes
148 in the strength, manufacturer, type (for example: Regular, NPH, Lente[®]), species
149 (beef, pork, beef-pork, human) or method of manufacture (recombinant [rDNA] or
150 animal source insulin) may cause a need for a change in the timing or dose of the new
151 insulin.
- 152 • Glucose monitoring will help you and your health care provider adjust dosages.
- 153 • Always carry a quick source of sugar, such as candy or glucose tablets, to treat low
154 blood sugars (hypoglycemia).
- 155 • Always carry identification that states that you have diabetes.

156

157 **What should I know about using NovoLog?**

158 *See the end of this Patient Information for instructions for using NovoLog in*
159 *injections and pumps.*

160

- 161 • NovoLog starts working 10-20 minutes after injection or infusion. The greatest blood
162 sugar lowering effect is between 1 and 3 hours after injection or infusion. This blood
163 sugar lowering lasts for 3 to 5 hours. (The time periods are only general guidelines.)
- 164
- 165 • Because the onset of action is rapid, you should eat a meal within 5-10 minutes after a
166 NovoLog injection or a NovoLog bolus dose from an external pump to avoid low
167 blood sugar (hypoglycemia).
- 168
- 169 • The shorter duration of NovoLog's action means that you may need to use an
170 intermediate or longer-acting insulin (basal insulin) or higher basal rates of NovoLog
171 insulin infusion in the pump. This will help you avoid hyperglycemia and
172 ketoacidosis.
- 173
- 174 • Do not inject or infuse in skin that has become reddened or bumpy or thickened after
175 infusion or injection. Insulin absorption in these areas may not be the same as that in
176 normal skin, and may change the onset and duration of insulin action.
- 177
- 178 • Use NovoLog only if it appears clear and colorless. Do not use NovoLog if it appears
179 cloudy, thickened, or colored, or if it contains solid particles.

180

181 **What should I avoid while using NovoLog?**

- 182 • Drinking alcohol may lead to hypoglycemia.
183 • Do not miss meals after injections of NovoLog or bolus infusions of NovoLog.

184

185 **What are the possible side effects of NovoLog?**

186 Insulins can cause hypoglycemia (low blood sugar), hyperglycemia (high blood sugar),
187 allergy, and skin reactions.

188

189 **Hypoglycemia** (insulin reaction). This is the most common side effect. It occurs when
190 there is a conflict between the amount of carbohydrates (source of glucose) from your
191 food, the amount of glucose used by your body, and the amount and timing of insulin
192 dosing. Therefore, **hypoglycemia can occur with:**

- 193 • **The wrong insulin dose.** This can happen with any of the following:
194 • too much insulin is injected
195 • the bolus dose of insulin infusion is set too high
196 • the basal infusion dose is set too high
197 • the pump does not work right, delivering too much insulin
198 • **Medicines that directly lower glucose or increase sensitivity to insulin.** This can
199 happen with oral (taken by mouth) antidiabetes drugs, sulfa antibiotics (for
200 infections), ACE inhibitors (for blood pressure and heart failure), salicylates,
201 including aspirin and NSAIDS (for pain), some antidepressants, and with other
202 medicines.
203 • **Medical conditions that limit the body's glucose reserve, lengthen the time**
204 **insulin stays in the body, or that increase sensitivity to insulin.** These conditions
205 include diseases of the adrenal glands, the pituitary, the thyroid gland, the liver, and
206 the kidney.
207 • **Not enough carbohydrate (sugar or starch) intake.** This can happen if:
208 • a meal or snack is missed or delayed
209 • you have vomiting or diarrhea that decreases the amount of glucose absorbed by
210 your body
211 • alcohol interferes with carbohydrate metabolism
212 • **Too much glucose use by the body.** This can happen from:
213 • too much exercise
214 • higher than normal metabolism rates due to fever or an overactive thyroid

215

216 Hypoglycemia can be mild or severe. Its onset may be rapid. Patients with very good
217 (tight) glucose control, patients with diabetic neuropathy (nerve problems), or patients
218 using some Beta-blockers (used for high blood pressure and heart conditions) may have
219 few warning symptoms before severe hypoglycemia develops. Hypoglycemia may reduce
220 your ability to drive a car or use mechanical equipment without risk of injury to yourself
221 or others. Severe hypoglycemia can cause temporary or permanent harm to your heart or
222 brain. **It may cause unconsciousness, seizures, or death.** Symptoms of hypoglycemia
223 include:

- 224 • anxiety, irritability, restlessness, trouble concentrating, personality changes, mood
- 225 changes, or other abnormal behavior
- 226 • tingling in your hands, feet, lips, or tongue
- 227 • dizziness, light-headedness, or drowsiness
- 228 • nightmares or trouble sleeping
- 229 • headache
- 230 • blurred vision or slurred speech
- 231 • palpitations (rapid heart beat)
- 232 • sweating
- 233 • tremor (shaking) or unsteady gait (walking)

234

235 Mild to moderate hypoglycemia can be treated by eating or drinking carbohydrates (milk,
236 orange juice, sugar candies, or glucose tablets). More severe or continuing hypoglycemia
237 may require the help of another person or emergency medical personnel. Patients who are
238 unable to take sugar by mouth or who are unconscious may need treatment with a
239 glucagon injection or glucose given intravenously (in the vein).

240

241 Talk with your doctor about severe, continuing, or frequent hypoglycemia, and
242 hypoglycemia for which you had few warning symptoms.

243

244 **Hyperglycemia** (high blood sugar) is another common side effect. It also occurs when
245 there is a conflict between the amount of carbohydrates (source of glucose) from your
246 food, the amount of glucose used by your body, and the amount and timing of insulin
247 dosing. Therefore, **hyperglycemia can occur with:**

- 248 • **The wrong insulin dose.** This can happen from any of the following:
 - 249 • too little or no insulin is injected
 - 250 • the bolus dose of insulin infusion is set too low
 - 251 • the basal infusion dose is set too low
 - 252 • the pump or catheter system does not work right, delivering too little insulin
 - 253 • the insulin's ability to lower glucose is changed by incorrect storage (freezing,
254 excessive heat), or usage after the expiration date
- 255 • **Medicines that directly increase glucose or decrease sensitivity to insulin.** This
256 can happen, for example, with thiazide water pills (used for blood pressure),
257 corticosteroids, birth control pills, and protease inhibitors (used for AIDS).
- 258 • **Medical conditions that increase the body's production of glucose or decrease**
259 **sensitivity to insulin.** These medical conditions include fevers, infections, heart
260 attacks, and stress.
- 261 • **Too much carbohydrate intake.** This can happen if you
 - 262 • eat larger meals
 - 263 • eat more often
 - 264 • increase the proportion of carbohydrate in your meals

265

266 Hyperglycemia can be mild or severe. It can **progress to diabetic acidosis (DKA)**
267 **(ketoacidosis) or very high glucose levels (hyperosmolar coma) and result in**

268 **unconsciousness and death.** Although diabetic acidosis occurs most often in patients
269 with Type 1 diabetes, it can occur in patients with Type 2 diabetes who become severely
270 ill. Urine or blood tests will show acetone, ketones, and high levels of glucose.

271 Hyperosmolar coma occurs most often in patients with Type 2 diabetes. Urine and blood
272 tests will show very high levels of glucose.

273 Glucose monitoring is very important for patients using external pump infusion therapy.

274 You should be aware that pump or infusion set malfunctions that result in inadequate
275 insulin infusion can quickly lead to hyperglycemia and ketosis. Accordingly, problems
276 with the infusion pump, the flow of insulin, or the quality of the insulin should be
277 identified and corrected as quickly as possible. The faster absorption of rapid-acting
278 insulin analogs through the skin and shorter duration of action may give you less time to
279 identify and correct the problem.

280 Because some patients experience few symptoms of hyperglycemia and ketosis, it is
281 important to monitor your glucose several times a day. Symptoms of hyperglycemia
282 include:

- 283 • confusion or drowsiness
- 284 • fruity smelling breath
- 285 • rapid, deep breathing
- 286 • increased thirst
- 287 • decreased appetite, nausea, or vomiting
- 288 • abdominal (stomach area) pain
- 289 • rapid heart rate
- 290 • increased urination and dehydration (too little fluid in your body)

291

292 Mild hyperglycemia can be treated by extra doses of insulin and drinking fluids
293 (rehydration). Patients using pumps should check pump function and replace the insulin
294 in the reservoir-syringe, as well as change the tubing and catheter and the infusion site.

295 **Patients using pumps may need to resume insulin injections with syringes or**
296 **injection pens.** Glucose and acetone-ketone levels should be monitored more often until
297 they return to normal. **More severe or continuing hyperglycemia requires prompt**
298 **evaluation and treatment by your health care provider.**

299

300 **Allergy can be serious.** Generalized allergy is an uncommon, but possibly life-
301 threatening, reaction to insulin products. Symptoms include:

- 302 • itchy rash over the entire body
- 303 • shortness of breath or wheezing
- 304 • confusion
- 305 • low blood pressure
- 306 • rapid heart beat
- 307 • sweating

308 **If you think you are having a generalized allergic reaction, get emergency medical**
309 **help right away.**

310

311 Allergic reactions at the injection site (itching, redness, hardness, or swelling) are more
312 common than generalized allergy. They may need several days or weeks to clear up.

313 Pump patients with site reactions may need to change their infusion sites more often than
314 every 48 hours. Patients should avoid injection or infusion of insulin into skin areas that
315 have reactions. Tell your doctor about such reactions, because they can become more
316 severe, or they may change the absorption of insulin.

317

318 **Lipodystrophy** is a common change in the fat below the injection site. These changes
319 include loss of fat (depressions in the skin called lipoatrophy) or thickening of the tissue
320 under the skin (lipohypertrophy). Pump patients with lipodystrophy may need to change
321 their infusion sites more often than every 48 hours. Patients should avoid injection or
322 infusion of insulin into skin areas that have these reactions. Tell your doctor about such
323 reactions because they can become more severe, or they may change the absorption of
324 insulin.

325

326 **How should I store NovoLog?**

- 327 • **NovoLog can be damaged by high temperatures.** Therefore, be sure to protect it
328 from high air temperatures, heat from the sun, saunas, long showers, and other heat
329 sources. This is especially important if you use a pump or an insulin pen, because
330 you carry these devices with you and they may be exposed to different temperatures
331 as you go about your daily activities. **Throw NovoLog away if it has been in**
332 **temperatures greater than 98.6°F (37°C).**
- 333
- 334 • **Unopened NovoLog** should be stored in a refrigerator but not in the freezer and
335 protected from light. Even if it has been refrigerated and protected from sunlight and
336 unopened, it should not be used after the expiration date on the label and the carton.
337 Unopened vials and cartridges can be stored unrefrigerated at temperatures below
338 86°F (30°C) and protected from light for up to 28 days.
- 339
- 340 • **Punctured vials and cartridges** can be stored unrefrigerated at temperatures below
341 86°F (30°C) and protected from light for up to 28 days. Punctured vials may be
342 stored in the refrigerator. Cartridges inserted into their NovoPen[®] 3 device should not
343 be stored in the refrigerator.
- 344
- 345 • **The NovoLog in the pump reservoir and the complete infusion set** (reservoir,
346 tubing, catheter-needle) should be replaced **at least every 48 hours.** Replacement
347 should be more often than every 48 hours if you have hyperglycemia, the pump alarm
348 sounds, or the insulin flow is blocked (occlusion).
- 349
- 350 • Never use NovoLog if it has been stored improperly.

351

352 **General advice**

353 This leaflet summarizes the most important information about NovoLog. If you would
354 like more information, talk with your doctor. You can ask your pharmacist or doctor for
355 information about NovoLog that is written for health professionals.

356

357 **Injection and pump infusion instructions**

- 358 • NovoLog comes in 10 mL (milliliter) vials or in 3 mL cartridges. NovoLog can be
359 withdrawn from vials with syringes for injection or for insertion into the reservoirs of
360 external subcutaneous infusion pumps (Disetronic H-TRON[®] plus V100 or MiniMed
361 Models 505, 506, or 507).
- 362 • Doses of insulin are measured in units. NovoLog is available as a U-100 insulin.
363 One milliliter (mL) of U-100 contains 100 units of insulin aspart (1 mL=1 cc). Only
364 U-100 type syringes should be used for injection to ensure proper dosing.
- 365 • Disposable syringes and needles are sterile if the package is sealed. They should be
366 used only once and thrown away properly, to protect others from harm.
- 367 • NovoLog PenFill[®] 3 mL cartridges are for use with the NovoPen 3, NovoPen 3 Demi,
368 and NovoPen Junior Insulin Delivery Devices and NovoFine[®] disposable needles.
369 Never share needles.

370

371 **How should I inject NovoLog?**

372

373 *Using Vials*

- 374 1. The vial and the insulin should be inspected. The insulin should be clear and colorless.
375 The tamper-resistant cap should be in place to be removed by you. If the cap had been
376 removed before your first use of the vial, or if the insulin is cloudy or colored, you
377 should return the vial to the pharmacy. Do not use it.
- 378 2. Both the injection site and your hands should be cleaned with soap and water or with
379 alcohol. The injection site should be dry before you inject.
- 380 3. The rubber stopper should be wiped with an alcohol wipe.
- 381 4. The plunger of the syringe should be pulled back until the black tip is at the level for
382 the number of units to be injected.
- 383 5. Insert the needle of the syringe through the rubber stopper of the vial. Push in the
384 syringe plunger completely to put air into the vial.
- 385 6. Turn the vial upside-down with the needle-syringe still attached, and pull the plunger
386 back a few units past the correct dose.
- 387 7. Remove any air bubbles by flicking the syringe and squirting air bubbles out the
388 needle. Continue pushing the plunger until you have the correct dose.
- 389 8. Lift the vial off the syringe.
- 390 9. Inject NovoLog into the subcutaneous (under the skin) tissue (not into muscle or
391 blood vessels) in the abdomen, thighs, upper arms, or buttocks. Pinch the skin fold
392 between your fingers and push the needle straight into the pinched skin. Because
393 insulin absorption and activity can be affected by the site you choose, you should
394 discuss the injection site with your doctor.
- 395 10. Release the pinched skin and push the plunger in completely. Keep the needle in the
396 skin for a few seconds before withdrawing the syringe.
- 397 11. Press the injection site for a few seconds to reduce bleeding. Do not rub.
- 398 12. To avoid needle sticks, throw away the syringe and needle without recapping. Discuss
399 sterile technique and proper disposal of your used insulin supplies with your doctor.

400

401 *Using Cartridges*

- 402 1. The cartridge and the insulin should be inspected. The insulin should be clear and
403 colorless. The tamper-resistant foil should be in place to be removed by you. If the
404 foil had been punctured or removed before your first use of the cartridge or if the
405 insulin is cloudy or colored, you should return the cartridge to the pharmacy. Do not
406 use it.
- 407 2. Both the injection site and your hands should be cleaned with soap and water or with
408 alcohol. The injection site should be dry before you inject. Do not use skin that is
409 reddened, itchy, or thickened as an infusion site.
- 410 3. Insert a 3 mL cartridge in the pen-device barrel. Attach a new needle to the end of the
411 cartridge and turn the pen device upside-down so that any air bubbles can be
412 eliminated by flicking the pen device and squirting air bubbles out the needle. (This
413 should eliminate extra air for all future doses from that cartridge. However, the needle
414 will need to be changed for each dose.)
- 415 4. Set the dose to be delivered by twisting the top of the pen-device until the correct
416 number appears in the window.
- 417 5. Inject NovoLog into the subcutaneous (under the skin) tissue (not into muscle or
418 blood vessels) in the abdomen, thighs, upper arms, or buttocks. Pinch the skin fold
419 between your fingers and push the needle straight into the pinched skin. Because
420 insulin absorption and activity can be affected by the site you choose, you should
421 discuss the injection site with your doctor.
- 422 6. Release the pinched skin. Inject the dose by pressing the flat plunger button on the
423 top of the pen-device. Keep the needle in the skin for a few seconds before
424 withdrawing the pen-device.
- 425 7. Press the injection site for a few seconds to reduce bleeding. Do not rub.
- 426 8. Throw away the disposable needle without recapping to avoid needle sticks. Discuss
427 sterile technique and proper disposal of your used insulin supplies with your doctor.
- 428

429 **How should I infuse NovoLog with an external subcutaneous insulin infusion pump?**

430

431 NovoLog is recommended for use with the Disetronic H-TRON[®] plus V100 and
432 MiniMed 505, 506, and 507 pumps. The Disetronic 3.15 plastic cartridge and Tenders or
433 Classic tubing can be used with the Disetronic pump. The MiniMed 3 mL syringe and
434 Polyfin[®] or Sof-set[®] tubing can be used in the MiniMed pumps. The use of NovoLog in
435 quick-release infusion sets and cartridge adapters has not been assessed.

436

- 437 1. Inspect your insulin as you would for an injection. The insulin should be clear and
438 colorless and without particles. The tamper-resistant cap should be in place to be
439 removed by you. If the cap had been removed before your first use of the vial or if the
440 insulin is cloudy or colored, you should return the vial to the pharmacy. Do not use it.
- 441 2. Both the infusion site and your hands should be cleaned with soap and water or with
442 alcohol. The infusion site should be dry before you insert the catheter-needle and
443 tubing. Do not use skin that is reddened, itchy, bumpy or thickened as an infusion site
444 because the onset and duration of NovoLog action may not be the same as that in
445 normal skin.

- 446 3. Fill the reservoir-syringe with 2 days worth of NovoLog plus about 25 extra units to
447 prime the pump and fill up the dead space of the infusion tubing.
- 448 4. Remove air bubbles from the reservoir according to the pump manufacturers'
449 instructions.
- 450 5. Attach the infusion set to the reservoir. Make sure the connection is tight. Prime the
451 infusion set until you see a drop of insulin coming out of the infusion needle-catheter.
452 Flick the tubing to remove air bubbles. Follow the pump manufacturers' instructions
453 for additional priming.
- 454 6. Prime the needle-catheter and insert the infusion set into the skin according to the
455 pump manufacturer.
- 456 7. Program the pump for mealtime NovoLog boluses and NovoLog basal insulin
457 infusion according to instructions from your doctor and the manufacturer of your
458 pump equipment.
- 459 8. Change the infusion site, the insulin reservoir, the tubing, the catheter-needle, and the
460 insulin every 48 hours or less, even if you have not used all of the insulin. This will
461 help ensure that NovoLog and the pump works well. (See "What is the most
462 important information I should know about NovoLog?")
- 463 9. Change the infusion site, the insulin reservoir, the tubing, the catheter-needle, and the
464 insulin if you experience a pump alarm, catheter blockage, hyperglycemia, or if your
465 pump insulin has been exposed to heat greater than 98.6°F (37°C). (See "What is the
466 most important information I should know about NovoLog?") Hyperglycemia
467 identified with glucose monitoring may be the first indication of a problem with the
468 pump, infusion set, or NovoLog. Hyperglycemia in the absence of an alarm still
469 requires you to investigate because pump alarms are designed to detect back-pressure
470 and occlusion. The alarms may not detect all the changes to NovoLog that could
471 result in hyperglycemia. You may need to resume subcutaneous insulin injections if
472 the cause of the problem cannot be promptly identified or fixed. (See
473 "Hyperglycemia" under "What are the possible side effects of NovoLog?")
474 Remember that long stretches of tubing increase the risk for kinking and expose the
475 insulin in the tubing to more variations in temperature.

476
477 **These instructions give you specific information for use of NovoLog in external**
478 **subcutaneous infusion pumps, but are not a substitute for pump education.**

479
480 *How should I mix insulins?*

481
482 **NovoLog should be mixed only when syringe injections are used.** NovoLog can be
483 mixed with NPH human insulin immediately before use. The NovoLog should be drawn
484 into the syringe before the NPH. Mixing with other insulins has not been studied.

485 **NovoLog should not be mixed with Lantus® (insulin glargine [rDNA origin]**
486 **injection). Mixed insulins should NEVER be used in a pump or for intravenous**
487 **infusion.**

- 488
489 1. Add together the doses of NPH and NovoLog. The total dose will determine the final
490 volume in the syringe after drawing up both insulins into the syringe.
- 491 2. Roll the NPH vial between your hands until the liquid is equally cloudy throughout.

- 492 3. Draw into the syringe the same amount of air as the NPH dose. Inject this air into the
493 NPH vial and then remove the needle without withdrawing or touching any of the
494 NPH insulin. (Transferring NPH to the NovoLog vial will contaminate the NovoLog
495 vial and may change how quickly it works.)
- 496 4. Draw into the syringe the same amount of air as the NovoLog dose. Inject this air into
497 the NovoLog vial. With the needle in place, turn the vial upside-down and withdraw
498 the correct dose of NovoLog. The tip of the needle must be in the NovoLog to get the
499 full dose and not an air dose.
- 500 5. Insert the needle into the NPH vial. Turn the NPH vial upside down with the syringe-
501 needle still in it. Withdraw the correct dose of NPH.
- 502 6. Inject immediately to reduce changes in how quickly the insulin works.

503

504

505 Helpful information for people with diabetes is published by the American Diabetes
506 Association, 1660 Duke Street, Alexandria, VA 22314

507

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519 License under U.S. Patent No. 5,618,913 and Des. 347,894

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