

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **PALYNZIQ**[®]

pegvaliase injection

Read this carefully before you start taking **Palynziq**[®] and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Palynziq**.

Serious Warnings and Precautions

- Palynziq can cause severe allergic reactions that may be life threatening and these can happen any time after a Palynziq injection. Stop injecting Palynziq and get emergency medical care right away if you have any of the following symptoms of a severe allergic reaction during treatment with Palynziq:
 - Swelling of the face, eyes, lips, mouth, throat, tongue, hands and/or feet
 - Trouble breathing or wheezing
 - Throat tightness or a choking feeling
 - Trouble swallowing or speaking
 - Feeling dizzy or fainting
 - Losing control of urine or stools
 - Rapid heartbeat
 - Hives (like an itchy, bumpy skin rash) that spreads quickly
 - Flushing
 - Severe stomach cramps or pain, vomiting, or diarrhea
- Your doctor will prescribe an epinephrine injection device to use in case of a severe allergic reaction. Your doctor will train and instruct you and someone helping you on when and how to use epinephrine. Keep the epinephrine injection device with you at all times.
- Your doctor may stop your treatment with Palynziq if you experience a severe allergic reaction or repeated episodes of a mild to moderate allergic reaction.

What is Palynziq used for?

Palynziq is a treatment for patients aged 16 years and older with phenylketonuria (PKU), a rare inherited disorder that causes phenylalanine from proteins in food to build up in the body. People who have PKU have high levels of phenylalanine and this can lead to serious health problems. Palynziq reduces the levels of phenylalanine in the blood of patients who have PKU whose blood phenylalanine levels cannot be kept below 600 micromol/l by other means such as by diet.

How does Palynziq work?

Palynziq contains the active substance pegvaliase, an enzyme that can break down phenylalanine in the body.

What are the ingredients in Palynziq?

Medicinal ingredients: pegvaliase

Non-medicinal ingredients: Sodium chloride, *trans*-cinnamic acid, trometamol, trometamol hydrochloride, water for injection.

Palynziq comes in the following dosage forms:

Solution for Injection in pre-filled syringe: 2.5 milligrams (mg) (white plunger), 10 mg (green plunger), 20 mg (blue plunger).

Do not use Palynziq if:

You have a severe allergy to pegvaliase or any other ingredients of this medicine, or another medicine that contains polyethylene glycol (PEG) [listed in the list of ingredients for other medicines and in this leaflet (What are the ingredients in Palynziq?)].

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Palynziq. Talk about any health conditions or problems you may have, including if you:

- Cannot or are not willing to use auto-injectable epinephrine to treat a severe allergic reaction.
- Have ever had a severe allergic reaction to polyethylene glycol (PEG).
- Are pregnant, think you may be pregnant, or are planning to become pregnant. Palynziq may harm your unborn baby and use of Palynziq during pregnancy is not recommended. You should use effective birth control when taking Palynziq and for at least 1 month after your last dose of Palynziq. Tell your healthcare professional right away if you become pregnant or think you might be pregnant while taking Palynziq.
 - If your phenylalanine levels are too high or too low during pregnancy, this may also affect your unborn baby. You and your healthcare professional can decide the best way for you to manage your blood phenylalanine levels. It is very important to keep your blood phenylalanine levels in the range your healthcare professional recommends during pregnancy.
 - There is a pregnancy registry that your healthcare professional can contact if you are pregnant. A pregnancy registry is a large database maintained by BioMarin to collect data on pregnant women taking Palynziq.
- Are breastfeeding or plan to breastfeed. Palynziq may pass into your breast milk. Talk to your healthcare professional about the best way to feed your baby if you take Palynziq.

To obtain additional information, refer to the Patient Medication Materials specific to pregnancy available at www.BioMarin.ca.

Other warnings you should know about:

You may have allergic reactions when being treated with Palynziq. Your doctor will tell you how to manage your allergic reactions based on the severity of the reaction and will prescribe you additional medicines to manage the reaction.

Give yourself time after taking Palynziq to see how you feel before driving a vehicle or using machinery.

If you stop taking Palynziq treatment, your blood phenylalanine levels are likely to increase. Talk to your doctor before stopping Palynziq treatment.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Palynziq:

- Injection of other medicines that contain PEG while using Palynziq: Palynziq contains an ingredient called polyethylene glycol (PEG). If you inject Palynziq around the same time as another injectable medicine that contains PEG, such as PEGylated medroxyprogesterone acetate, you may have an allergic reaction. Tell your doctor or pharmacist if you are injecting, have recently injected or might inject any other medicines.
- There have been no studies testing how Palynziq interacts with other drugs or products.

Patient Education materials have been developed to help you understand allergic reactions and what to do in case of severe allergic reaction that can be found at www.BioMarin.ca.

How to take Palynziq:

Take Palynziq exactly as your doctor or healthcare professional has told you.

Palynziq is given as an injection under the skin (subcutaneous injection).

Be sure that you know from your healthcare professional the dose of Palynziq that you need to use and whether you need to use Palynziq 2.5 mg syringe (white plunger), 10 mg syringe (green plunger), 20 mg syringe (blue plunger), or a combination of syringes to make the dose.

Preparing the dose of Palynziq:

- You will start Palynziq at the lowest dose. You will use the 2.5 mg syringe once a week for at least the first 4 weeks. The 2.5 mg syringe has a white plunger.
- Your doctor will then slowly increase your dose and/or how often you inject Palynziq. Your doctor will tell you how long to stay at each dose. Slowly increasing your dose over time allows your body to adjust to this medicine.
- The goal is to reach a daily dose that lowers your blood phenylalanine levels to ≤ 600 micromol/l and does not cause too many side effects. You may need a daily dose of 20 mg, 40 mg, or 60 mg to reach your target blood phenylalanine level.

Example of steps to reach your blood phenylalanine goal

Palynziq dose and how often to take it	Syringe color
2.5 mg once a week	White plunger
2.5 mg two times a week	
10 mg once a week	Green plunger
10 mg twice a week	
10 mg four times a week	
10 mg daily	
20 mg daily	Blue plunger
40 mg daily (2 injections of 20 mg pre-filled syringe) ¹	
60 mg daily (3 injections of 20 mg pre-filled syringe) ¹	

¹ If you need more than one injection to receive your daily dose, all injections should be done at the same time of day and injection sites should be at least 5 centimeters away from each other. Do not divide your daily dose throughout the day.

- Your doctor will continue to check your blood phenylalanine levels during treatment to see if this medicine is working for you and may adjust your dose of Palynziq or ask you to change your diet.

Starting Palynziq:

- Your healthcare professional will give you the Palynziq injection until you (or a caregiver) can do it yourself.
- Your doctor will prescribe medicines for you to take before your Palynziq injection, such as acetaminophen, fexofenadine, and/or ranitidine. These medicines may help to reduce the symptoms of an allergic reaction.
- A healthcare professional will monitor you for at least 1 hour after you get Palynziq for signs and symptoms of an allergic reaction.
- Your doctor will prescribe an epinephrine injection device to use for any severe allergic reactions. Your healthcare professional will also tell you the signs and symptoms to look out for and what to do if you have a severe allergic reaction.
- Your doctor will show you how and when to use the epinephrine injection device. Keep it with you at all times.

Continuing Palynziq:

- This medicine comes in prefilled syringes with 3 different strengths (2.5 mg white plunger, 10 mg green plunger, or 20 mg blue plunger). You may need more than one prefilled syringe for your

prescribed dose. Your healthcare professional will tell you which syringe, or a combination of syringes, to use and will show you (or a caregiver) how to inject Palynziq.

- The “Instructions for Use” shows you:
 - how to prepare and inject Palynziq and
 - how to throw away Palynziq syringes properly after you use them
- Your doctor will tell you how long to continue taking medicines such as acetaminophen, fexofenadine, and/or ranitidine before you take Palynziq.
- For at least the first 6 months of Palynziq treatment after you started receiving the injection at home, you must have an adult trained observer with you when injecting Palynziq, and for at least 1 hour after your injection to watch for signs and symptoms of a severe allergic reaction and, if needed, give you an injection of epinephrine and call for emergency medical help.
 - Your doctor will train the caregiver/observer on the signs and symptoms of a severe allergic reaction and how to give an injection of epinephrine.
 - Your doctor will tell you if you need an observer for longer than 6 months.
- Do not change your protein intake unless your doctor tells you to.

Overdose:

If you think you, or a person you are caring for, have taken too much Palynziq, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you missed a dose of this medication, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and continue with your next scheduled dose. Go back to your regular dosing schedule. Do not take two doses at the same time.

What are possible side effects from using Palynziq?

These are not all the possible side effects you may have when taking Palynziq. If you experience any side effects not listed here, tell your healthcare professional.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON			
Sudden severe allergic reaction: <ul style="list-style-type: none"> • Swelling of the face, eyes, lips, mouth, throat, tongue, hands and/or feet • Trouble breathing or wheezing • Throat tightness or a choking feeling • Trouble swallowing or speaking • Feeling dizzy or fainting • Losing control of urine or stools • Rapid heartbeat • Hives (like an itchy, bumpy skin rash) that spreads quickly • Flushing • Severe stomach cramps or pain, vomiting, or diarrhea 		✓	✓
RARE			
Serum sickness allergic reaction: combination of <ul style="list-style-type: none"> • Fever (high temperature) • Rash • Muscle and joint aches 		✓	

Other side effects with using Palynziq

Very common: may affect more than 1 in 10 people

- Feeling sick (also called nausea)
- Stomach pain
- Vomiting
- Allergic reactions occur very commonly and range in severity. Symptoms of an allergic reaction can include skin rash, itching, swelling of the head or face, itchy or runny eyes, cough, and wheezing.
- Skin redness
- Swelling
- Bruising
- Tenderness, or pain where you injected Palynziq
- Joint pain
- Muscle pain
- Headache
- Feeling dizzy
- Cough
- Skin rash
- Hives (raised itchy rash on the skin)
- Skin redness
- Itchiness
- Thinning or loss of hair
- Decrease in complement factors C3 and C4 proteins (which are involved in protecting against infections) in blood tests
- Increase in c-reactive protein (CRP) in blood tests (CRP is a protein that indicates that you have inflammation)
- Too low levels of phenylalanine in blood tests

Common (may affect up to 1 in 10 people)

- Swollen glands in the neck, armpit or groin
- Joint swelling
- Joint stiffness
- Muscle stiffness
- Skin rash with small bumps
- Blistering or peeling of the outer layer of the skin

Your healthcare professional will decide when to perform blood tests and will interpret the results.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store in a refrigerator (2 to 8°C). Do not freeze.
- If needed, you may store Palynziq in its sealed tray outside the refrigerator (20 to 25°C) for up to a single period of 30 days away from sources of heat. Record the date removed from refrigeration on the unopened product tray. Once stored outside of refrigeration, the product must not be returned to the refrigerator.
- Store in the original carton to protect from light.
- Do not keep Palynziq that is out of date, or that you no longer need.

Keep out of reach and sight of children.

If you want more information about Palynziq:

- Talk to your healthcare professional
- Go to the Patient Information Materials on BioMarin website at www.biomarin.ca
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>; or by calling 1-800-983-4587.

This leaflet was prepared by BioMarin International Limited.

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INSTRUCTIONS FOR USE

Read this Instructions for use before you start using the Palynziq pre-filled syringe and each time you get a new prescription. There may be new information. Also, talk to your healthcare professional about your medical condition or your treatment.

Follow these instructions carefully while you are using Palynziq. If your healthcare professional decides that you or your caregiver can give your injections of Palynziq at home, your healthcare professional will show you or your caregiver how to inject Palynziq before you inject it for the first time. **Do not** inject Palynziq until your healthcare professional has shown you or your caregiver how to inject Palynziq.

Talk to your healthcare professional if you have any questions about how to inject Palynziq the right way.

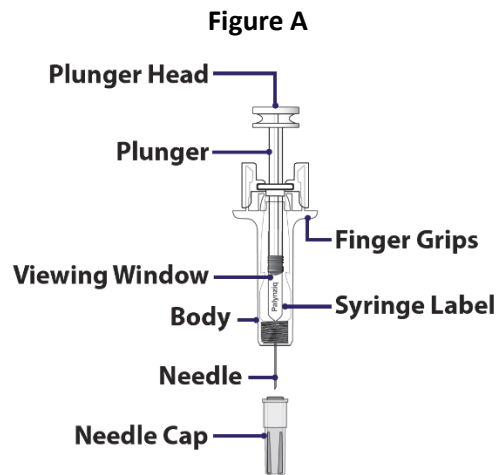
Do not share your pre-filled syringes with anyone else.

For storage instructions, refer to **STORAGE** in this leaflet.

Important things to know about using your Palynziq pre-filled syringe:

- Use each Palynziq pre-filled syringe once only. **Do not** use a Palynziq syringe more than once.
- **Never** pull back on the plunger.
- **Do not** remove the needle cap until you are ready to inject.

Figure A below shows what the pre-filled syringe looks like before use.



Select the correct Palynziq pre-filled syringe(s) for your dose:

When you receive your Palynziq pre-filled syringe(s), check that the name “Palynziq” appears on the carton(s).

- Palynziq pre-filled syringes come in 3 different strengths: 2.5 mg, 10 mg, and 20 mg.
- You may need more than one pre-filled syringe for your prescribed dose. Your healthcare professional will tell you which syringe, or combination of syringes, to use. Ask your healthcare professional if you have any questions.
- Before you inject Palynziq, check each carton and syringe to make sure you have the right pre-filled syringe for your prescribed dose.

Figure B

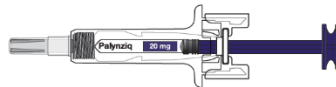
2.5 mg strength



10 mg strength



20 mg strength



PREPARING FOR INJECTION

Step 1: Collect supplies:

Gather your supplies for the injection and place them on a clean flat surface. Take out the required number of cartons needed for your dose from the refrigerator.

Supplies you will need for your Palynziq Injection:

- Palynziq pre-filled syringe(s) in sealed tray(s). Each tray contains 1 syringe.
- gauze pad or cotton ball
- 1 alcohol pad
- 1 bandage
- 1 sharps disposal or puncture resistant container

Step 2: Remove Palynziq tray(s) from carton and check expiry date:

- Take out the cartons needed for your dose from the refrigerator. Check the expiry date on the carton. If the expiry date has passed, do not use the pre-filled syringe in that carton.
- Open each carton and take out the sealed tray you need for your dose.
- Place each sealed tray on a clean, flat surface out of reach of children and pets.
- Put the carton with any remaining trays back in the refrigerator. If a refrigerator is not available, see section 5 “*How to store Palynziq*” in this leaflet.

Step 3: Allow Palynziq tray(s) to sit at room temperature for 30 minutes before opening:

Let the sealed tray(s) sit at room temperature for **at least 30 minutes**. Injecting cold Palynziq can be uncomfortable.

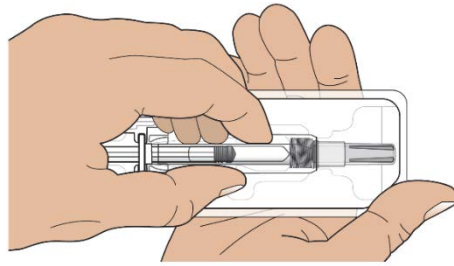
- **Do not** warm up the pre-filled syringe in any other way. **Do not** use a microwave and do not place in hot water.

Step 4: Remove syringe from tray:

Peel the cover from the tray. Hold the middle of the pre-filled syringe body and take out the pre-filled syringe from the tray (see Figure C).

- **Do not** use the pre-filled syringe if it looks damaged or used. Use a new pre-filled syringe for your injection.
- **Do not** remove the needle cap from your pre-filled syringe.
- **Do not** shake or roll the syringe in your hands.

Figure C

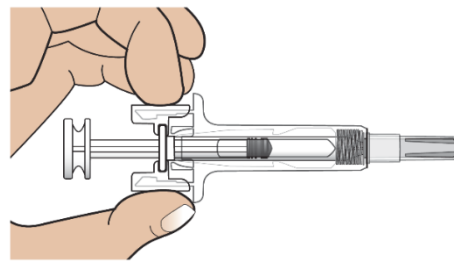


Step 5: Check syringe strength and check for particles:

Check the syringe label to make sure you have the correct strength for your prescribed dose. Look at the liquid through the viewing window (see Figure D). The liquid should look clear and colorless to pale yellow. It is normal to see an air bubble.

- **Do not** flick or try to push the bubble out.
- **Do not** use the pre-filled syringe if the liquid is cloudy, discolored, or has lumps or particles in it. Use a new pre-filled syringe for your injection.

Figure D



INJECTING PALYNZIQ

Step 6: Choose your injection site.

The recommended injection sites are:

- Front middle of the thighs.
- Lower part of the abdomen except for the 5 centimeter area around the belly button (navel).

If a caregiver is giving the injection, the top of the buttocks and the back of the upper arms may also be used (see Figure E).

Note:

- **Do not** inject into moles, scars, birthmarks, bruises, rashes, or areas where the skin is hard, tender, red, damaged, burned, inflamed, or tattooed.
- If you need more than 1 injection for your daily dose, the injection sites should be at least 5 centimeters away from each other (see Figures E and F).
- Each day, change (rotate) your injection sites. Choose an injection site that is at least 5 centimeters away from the injection site(s) you used the day before. It can be on the same part of the body or a different part of the body (see Figures E and F).

Step 7: Wash your hands well with soap and water (see Figure G).

Figure E

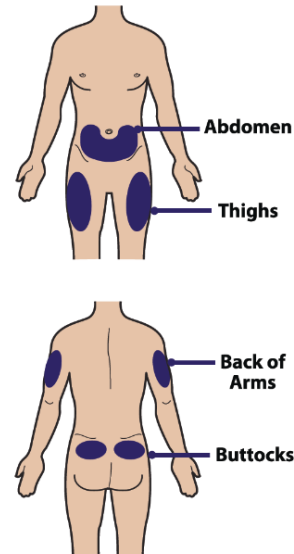


Figure F

Inject at least 5 cm apart

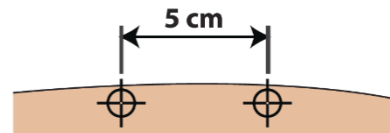


Figure G



Step 8: Clean the chosen site with an alcohol pad. Let the skin air dry for at least 10 seconds before injecting (see Figure H).

- **Do not** touch the cleaned injection site.
- **Do not** remove the needle cap until you are ready to inject Palynziq.
- Before injecting, check to make sure the needle is not damaged or bent.

Inject Palynziq

Step 9: Hold the body of the pre-filled syringe with one hand with the needle facing away from you (see Figure I).

- **Do not** use the pre-filled syringe if it has been dropped. Use a new pre-filled syringe for your injection.

Figure H

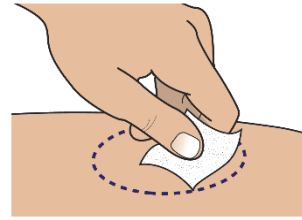
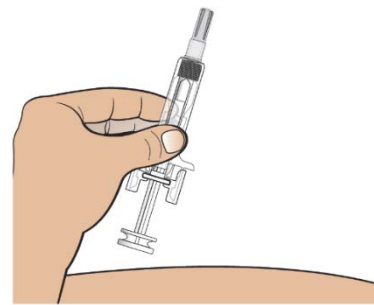


Figure I

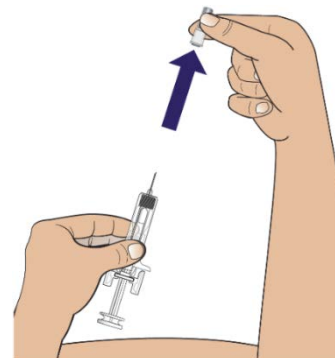


Step 10: Pull the needle cap straight off the needle (see Figure J).

- **Do not** twist the needle cap during removal.
- **Do not** hold the pre-filled syringe by the plunger or plunger head while taking the needle cap off.

You may see a drop of liquid on the tip of the needle. This is normal. **Do not** wipe it away. Throw the needle cap away in a sharps disposal or puncture-resistant container.

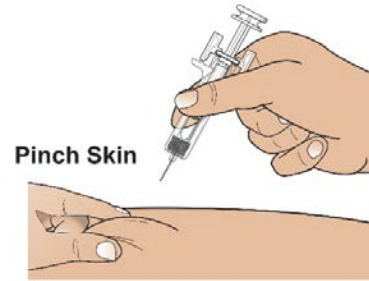
Figure J



Step 11: Hold the body of the pre-filled syringe in 1 hand between your thumb and index finger. Use your other hand to pinch up the skin around the injection site. Hold the skin firmly (see Figure K).

- **Do not** touch the plunger head while inserting the needle into the skin.

Figure K



Step 12: Use a quick motion to fully insert the needle into the pinched skin at a 45 to 90 degree angle (see Figure L).

Release the pinch of skin. Use that hand to hold the bottom of the syringe steady. Place the thumb of your other hand on the plunger head (see Figure L).

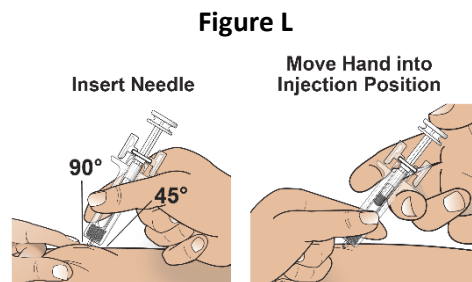


Figure L

Step 13: Use your thumb to push in the plunger slowly and steadily as far as it will go to inject all the medicine (see Figure M). More pressure may be needed to inject all the medicine for the 10 mg and 20 mg strengths.

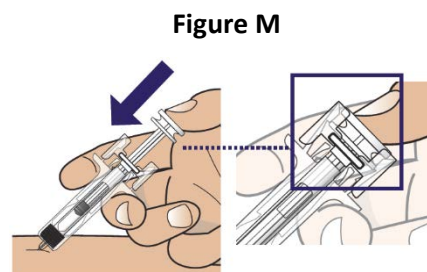


Figure M

Step 14: Slowly move your thumb up to release the plunger allowing the needle to automatically be covered by the syringe body (see Figure N).

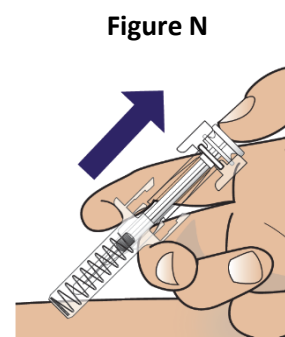


Figure N

Treat injection site

Step 15: Treat injection site (if needed).

If you see drops of blood at the injection site, press a sterile cotton ball or gauze over the injection site and hold for about 10 seconds. You may cover the injection site with an adhesive bandage if needed.

If more than one syringe is needed:

Step 16: If your health care professional tells you to use more than one syringe for your dose, repeat Steps 4 to 15 listed above for each syringe that you use.

- **Note: Do not** inject multiple injections in the same spot. The injection sites should be at least 5 centimeters away from each other. See Step 6 for choosing an injection site.
- If multiple syringes are needed for a single dose, you should inject at the same time of day. Doses should not be divided over the course of the day

If your dose requires more than one syringe, repeat Steps 4 to 15 immediately for each syringe you use.

Dispose of the used syringes

Put your used needles and syringes in a sharps disposal or puncture-resistant container right away after use. Check with your doctor, pharmacist or nurse about the right way to throw away the container. Use safe disposal procedures for syringes.