

Package leaflet: Information for the patient

Natpar 25 micrograms/dose powder and solvent for solution for injection
Natpar 50 micrograms/dose powder and solvent for solution for injection
Natpar 75 micrograms/dose powder and solvent for solution for injection
Natpar 100 micrograms/dose powder and solvent for solution for injection
Parathyroid hormone

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Natpar is and what it is used for
2. What you need to know before you use Natpar
3. How to use Natpar
4. Possible side effects
5. How to store Natpar
6. Contents of the pack and other information
7. Instructions for use

1. What Natpar is and what it is used for

What is Natpar?

Natpar is a hormone replacement for adults with under-active parathyroid glands, a condition known as 'hypoparathyroidism'.

Hypoparathyroidism is a disease caused by low levels of parathyroid hormone, which is produced by the parathyroid glands in the neck. This hormone controls the amount of calcium and phosphate in the blood and urine.

If your levels of parathyroid hormone are too low, you can have low blood calcium. Low calcium can cause symptoms in many parts of your body, including the bones, heart, skin, muscles, kidneys, brain and nerves. For a list of symptoms of low calcium, see section 4.

Natpar is a synthetic form of parathyroid hormone that helps you keep calcium and phosphate levels in your blood and urine at a normal level.

2. What you need to know before you use Natpar

Do not use Natpar

- if you are allergic to parathyroid hormone or any of the other ingredients of this medicine (listed in section 6)

- if you are having or have had radiation therapy to the skeleton
- if you have cancer of the bones or other cancer that has spread to your bones
- if you are at increased risk of developing a bone cancer called osteosarcoma (for instance, if you have Paget's disease or other bone diseases)
- if a blood test shows you have unexplained increases in bone alkaline phosphatase
- if you have pseudohypoparathyroidism, a rare condition where the body does not respond adequately to the parathyroid hormone produced by the body

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Natpar.

If you are treated with Natpar, you may have side effects related to low or high levels of calcium in your blood (see section 4 for these side effects).

These effects are more likely to occur:

- when first starting Natpar,
- if you change your Natpar dose,
- if you miss one of your daily injections,
- if you stop taking Natpar for a short time or altogether.

You may be given medicines to treat or help prevent these side effects, or you may be asked to stop some of the medicines you are taking. These medicines include calcium or vitamin D.

If your symptoms are severe, your doctor may give you additional medical treatment.

Your doctor will check your calcium levels. You may need to change your Natpar dose or stop the injections for a short time.

Tests and checks

Your doctor will check how you respond to the treatment:

- during the first 7 days of starting treatment and
- if your dose is changed.

This will be done using tests to measure the level of calcium in your blood or urine. Your doctor may tell you to change the amount of calcium or vitamin D you take (in any form, including foods rich in calcium).

Talk to your doctor or pharmacist before using Natpar if you suffer from kidney stones.

Children and adolescents

Natpar should not be used in children or adolescents under 18 years old.

Other medicines and Natpar

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including:

- digoxin, also known as digitalis, a heart medicine
- medicines used to treat osteoporosis, called bisphosphonates, such as alendronic acid
- medicines that can affect calcium levels in your blood such as lithium or some medicines used to increase the amount of urine (diuretics).

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. There is limited information on the

safety of Natpar in pregnant women. Natpar has been shown to pass into breast milk in rats, but it is not known if Natpar would pass into breast milk in humans.

Your doctor will decide whether to start treatment with Natpar. Your doctor will also decide if you should keep taking this medicine if you become pregnant or start breast-feeding while taking it.

It is not known if Natpar has any effects on fertility.

Driving and using machines

Natpar has no effect on your being able to drive or use machines. However, hypoparathyroidism itself may affect your ability to concentrate. If your ability to concentrate is impaired, you should not drive or use machines until your ability to concentrate is improved.

Natpar contains sodium

This medicinal product contains less than 1 mmol (23 mg) sodium per dose. This means that it is essentially “sodium-free”.

3. How to use Natpar

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. Your doctor or nurse will train you on how to use the Natpar pen.

Natpar is given as a subcutaneous (under the skin) injection every day, using a pen to help you inject your medicine.

The ‘Natpar reusable pen’ is called ‘Natpar pen’ or ‘pen’ in this leaflet.

Dose

The recommended starting dose of Natpar is 50 micrograms per day.

- However, your doctor may start you on 25 micrograms per day based on a blood test result.
- After 2 to 4 weeks, your doctor may adjust the dose.

The dose of Natpar varies from person to person. People may need between 25 and 100 micrograms of Natpar per day.

Your doctor may tell you to take other medicines such as calcium supplements or vitamin D while you are taking Natpar. Your doctor will tell you how much you should take each day.

How to use the pen

Read “**Section 7. Instructions for use**” in this leaflet before you use the pen.

Do not use the pen if the solution is cloudy or coloured or if it contains visible particles.

Before the pen is used for the first time, the medicine has to be mixed.

After you have mixed the medicine, the Natpar pen is ready for use and the medicine can be injected under the skin of your thigh. Inject in the other thigh the following day and continue to alternate between the two.

It is strongly recommended that every time you receive a dose of Natpar, the name and batch number of the product are recorded in order to maintain a record of the batches used.

How long to use

Keep using Natpar for as long as your doctor prescribes it for you.

If you use more Natpar than you should

If, by mistake, you inject more than one dose of Natpar in a day, contact your doctor or pharmacist immediately.

If you forget to use Natpar

If you forget to use Natpar (or cannot inject it at your usual time), use your injection as soon as you can but do not inject more than one dose in the same day.

Take your next dose of Natpar at the usual time the next day. You may need to take more calcium supplements if you have signs of low blood calcium; see section 4 for symptoms.

Do not inject a double dose to make up for a forgotten dose.

If you stop using Natpar

Discuss with your doctor if you want to stop treatment with Natpar.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects

The following potentially serious side effects can occur when using Natpar:

- Very common: high levels of calcium in your blood, which can occur more often when you start treatment with Natpar.
- Very common: low levels of calcium in your blood; this can occur more often if you suddenly stop taking Natpar.

Symptoms related to high or low calcium levels are included in the list below. If you experience any of these side effects, contact your doctor right away.

Other side effects include:

Very common (may affect more than 1 in 10 people):

- headaches^{*,†}
- tingling and numbness of the skin[†]
- diarrhoea^{*,†}
- nausea and vomiting^{*}
- joint pain^{*}
- muscle spasms[†]

Common (may affect up to 1 in 10 people):

- feeling nervous or anxious[†]
- sleep problems (feeling sleepy during the day or having trouble sleeping at night)^{*}
- fast or uneven heart beat^{*,†}
- high blood pressure^{*}

- cough[†]
- stomach pain*
- muscle twitching or cramping[†]
- pain in your muscles[†]
- neck pain[†]
- pain in your arms and legs
- increased level of calcium in your urine*
- need to pass urine often[†]
- fatigue and lack of energy*
- chest pain
- redness and pain at injection site
- thirst*
- antibodies (produced by your immune system) to Natpar
- in blood tests, your doctor may see decreased levels of vitamin D and magnesium[†]

Not known (frequency cannot be estimated from the available data):

- allergic reactions (hypersensitivity), such as: swelling of the face, lips, mouth, or tongue; shortness of breath; itching; rash; hives
- seizures (fits) due to low levels of calcium in your blood[†]

*These side effects may be related to high level of calcium in your blood.

[†]These side effects may be related to low level of calcium in your blood.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme at Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Natpar

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the cartridge and carton after EXP. The expiry date refers to the last day of that month.

Before mixing

- Store in a refrigerator (2°C to 8°C).
- Do not freeze.
- Keep the cartridge within its cartridge holder in the outer carton in order to protect from light.

After mixing

- Store in a refrigerator (2°C to 8°C).
- Do not freeze.
- Keep the pen containing a mixed cartridge tightly closed in order to protect from light.
- Do not use this medicine for more than 14 days after it has been mixed.
- Do not use this medicine if it has not been stored correctly.
- Before attaching a new needle to your Natpar pen, check that the solution is clear and colourless. It is common to see small bubbles. Do not use this medicine if it has become cloudy, coloured, or contains visible particles.

Do not throw away any medicines via household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Natpar contains

The active substance is parathyroid hormone (rDNA).

It is available in 4 different strengths of cartridge (each cartridge contains 14 doses):

Natpar 25 micrograms

Each dose contains 25 micrograms parathyroid hormone in 71.4 microlitre solution following reconstitution.

Natpar 50 micrograms

Each dose contains 50 micrograms parathyroid hormone in 71.4 microlitre solution following reconstitution.

Natpar 75 micrograms

Each dose contains 75 micrograms parathyroid hormone in 71.4 microlitre solution following reconstitution.

Natpar 100 micrograms

Each dose contains 100 micrograms parathyroid hormone in 71.4 microlitre solution following reconstitution.

The other ingredients in the cartridge (for all strengths) are:

In the powder:

- sodium chloride
- mannitol
- citric acid monohydrate
- sodium hydroxide (for pH adjustment)

In the solvent:

- metacresol
- water for injections

What Natpar looks like and contents of the pack

Each cartridge of Natpar contains medicine as a powder together with a solvent to make a solution for injection. The cartridge is made of glass, with a rubber seal on top. The cartridge is contained in a plastic cartridge holder.

Natpar is available in a pack with 2 cartridges inside their cartridge holders.

The carton/cartridge colour shows the strength of your Natpar medicine:

Natpar 25 micrograms/dose

Purple cartridge.

Natpar 50 micrograms/dose

Red cartridge.

Natpar 75 micrograms/dose

Grey cartridge.

Natpar 100 micrograms/dose
Blue cartridge.

Marketing Authorisation Holder and Manufacturer

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This leaflet was last revised in 02/2022.

This medicine has been given ‘conditional approval’. This means that there is more evidence to come about this medicine.

7. Instructions for use

This guide is designed to help you prepare, inject, and store your Natpar pen.

These instructions are divided into 5 stages

Getting to know the parts of your Natpar pen and your Natpar medicine
Preparing and mixing your Natpar
Preparing your Natpar pen
Giving your daily dose
How to store your medicine

If you require assistance at any time, contact your doctor, pharmacist or nurse.

You may also contact Takeda at +44(0) 3333 000181 or email at medinfoEMEA@takeda.com.

What you need to know before getting started

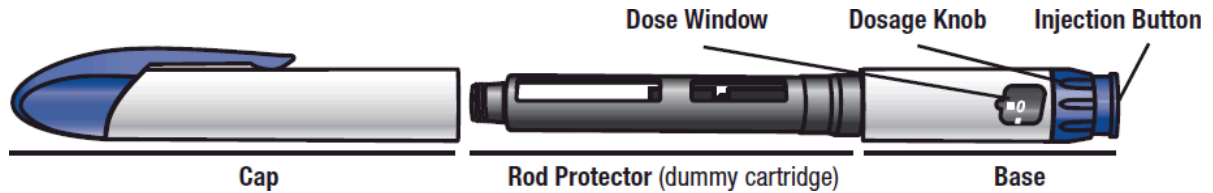
- Do NOT use your Natpar pen until your doctor or nurse has shown you how to use it.
- Use these instructions for use every time you mix your medicine, prepare your pen, or give an injection so you do not forget to do a step.
- A new needle must be attached to the pen every day.
- A new cartridge should be prepared once every 14 days.
- Do NOT use this medicine if you notice that it has become cloudy, coloured, or contain visible particles.
- Always store the cartridge in the refrigerator (at 2°C – 8°C).
- Do NOT freeze your cartridge.
- Do NOT use a cartridge that has been frozen.
- Discard all mixed cartridges older than 14 days.
- Only take your dose once per day.
- To clean your Natpar pen, wipe the outside of the pen with a damp cloth. DO NOT place the pen in water or wash or clean it with any liquid.
- Throw away the used Natpar cartridge and used needles as instructed by your doctor, pharmacist or nurse.
- Your Natpar pen can be re-used for up to 2 years

Getting to know the parts of your Natpar pen and your Natpar medicine

Get to know the Natpar pen components

Parts of your Natpar pen

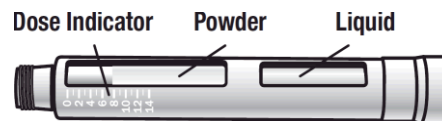
Note: The rod protector (dummy cartridge) protects the rod during shipment from the factory. Throw away the rod protector when you are ready to use your pen.



Your Natpar cartridge

Your Natpar cartridge contains medicine powder and solvent to mix the powder with. You must mix the powder and the solvent in the cartridge before using your Natpar pen.

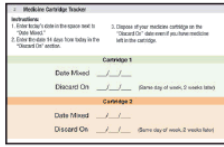
- Each cartridge contains **14** doses.
- The dose indicator shows you the number of doses left in the cartridge.



Other supplies that are needed:

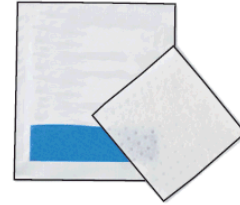
Note: The alcohol swabs, injection needles and the puncture resistant container are not included in the pack.

The Medicine Cartridge Tracker is located within this instructions for use.

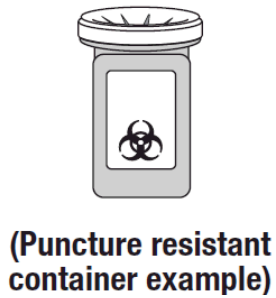
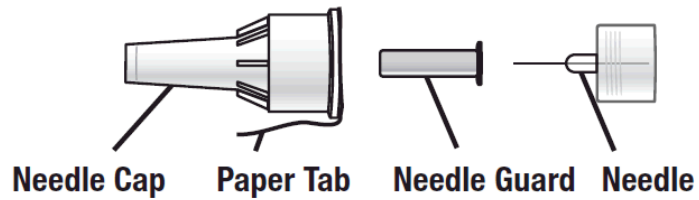


Medicine Cartridge Tracker

Use the **alcohol swab** to clean the injection area.

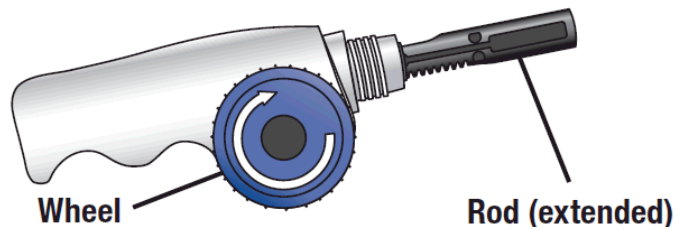


Disposable needle (Exploded view)



(Puncture resistant container example)

Mixing Device



Preparing and mixing your Natpar

You need to mix Natpar before you can use it. Once the medicine is mixed, it can be used for up to **14** injections (**14** doses).

If this is your first time using Natpar by yourself, your doctor or nurse will guide you through how to mix your Natpar cartridge.

1. When preparing to inject a dose, be sure to remove your Natpar cartridge from the refrigerator.

Note: You should store your cartridge in the refrigerator at all times, except when preparing and injecting your medicine.

- Wash and dry your hands.
- Gather your supplies, including:
 - Your mixing device
 - New Natpar cartridge from the refrigerator
 - New disposable pen needle
 - Puncture resistant sharps container
 - A pencil or pen to write the dates you mix your cartridge
 - Your medicine cartridge tracker (located within this instructions for use)
 - Your Natpar pen to inject your medicine
 - This instructions for use



2. Fill in the dates in your medicine cartridge tracker.

Medicine cartridge tracker

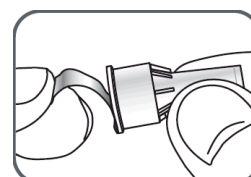
Instructions:

- Enter today's date in the space next to "**Date mixed.**"
- Enter the date **14** days from today in the space next to "**Discard on**" (Same day of the week, 2 weeks later).
- Dispose of your cartridge on the "**Discard on**" date even if you have medicine left in your cartridge. **Do not** use your cartridge on the "**Discard on**" date.
- A pen needle **must be** attached to mix a new cartridge.

Cartridge 1	
Date Mixed	___/___/___
Discard On	___/___/___ (Same day of week, 2 weeks later)

Cartridge 2	
Date Mixed	___/___/___
Discard On	___/___/___ (Same day of week, 2 weeks later)

3. Remove the paper tab from the needle cap.



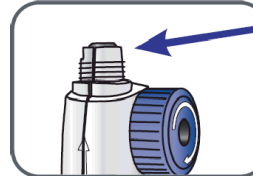
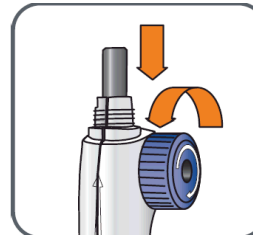
4. **Screw the Pen Needle onto the cartridge in a clockwise direction.**

- Ensure the Pen Needle is straight and tight on the cartridge (the wider edge of the needle cap must touch the ‘shoulder’ of the cartridge)
- **Do not** remove the needle cap or guard until you are ready to give your medicine.



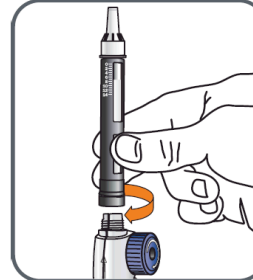
5. Turn the wheel of the mixing device in a counterclockwise direction to lower the rod if it is not already lowered.

- Make sure the rod in the mixing device looks like this (completely retracted).



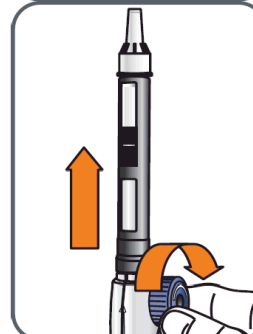
6. Screw the Natpar cartridge onto your mixing device in a clockwise direction.

- The pen needle must be firmly attached.



7. **With the needle cap pointing up**, turn the wheel slowly in a clockwise direction until the stoppers within the cartridge no longer move **and until the wheel turns freely**.

- Keep the needle pointing up.
- Do NOT hold the mixing device at an angle.

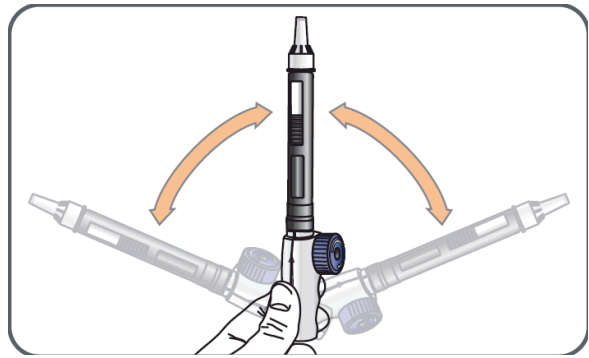


8. Make sure the stoppers look like this and stay together.



9. Hold the mixing device with the attached cartridge, with the needle pointed up, and **gently** move the cartridge from side to side (from 9 o'clock to 3 o'clock) about 10 times to **dissolve the powder** that is in the cartridge.

- **Do NOT shake the cartridge.**
- Ensure the needle is pointing up.
- Put the mixing device down with the cartridge attached and wait for 5 minutes to allow complete dissolution of the powder.

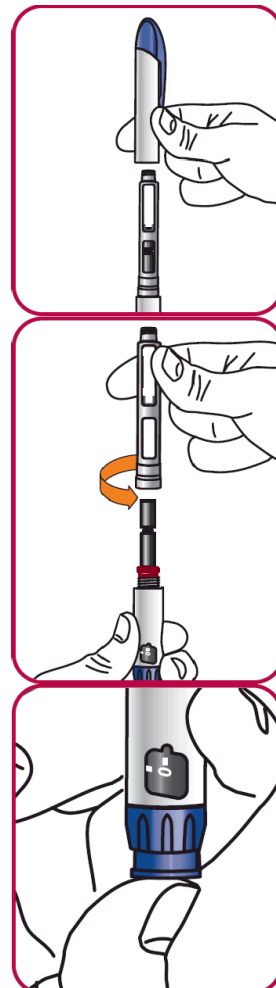


Check the solution before **giving every daily dose**. If the solution is cloudy, contains visible particles, or is not colourless after 5 minutes, **do not use this medicine**. **Contact your doctor, pharmacist or nurse**. It is normal to see small bubbles.

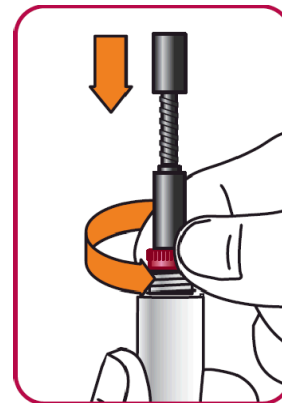
Preparing your Natpar pen

You will prepare your Natpar pen **once** every **14** days.

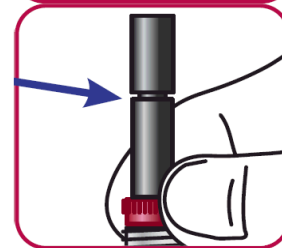
1. Pick up your pen and remove the cap. Save the cap for later use.
2. Unscrew the rod protector (**dummy cartridge**) or the empty medicine cartridge in a counterclockwise direction and throw it in a puncture resistant sharps container.
3. Press the injection button. You should see “0” line up with the notch in the dose window. If you do not see “0” line up, press the injection button until it is lined up.



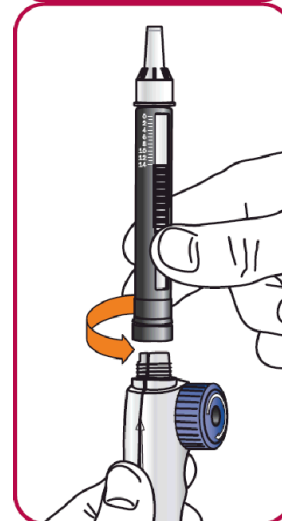
4. Lower the rod. If the rod is extended, turn the dark red ring counterclockwise to lower it. Do not tighten the ring too much.



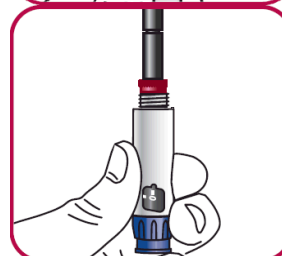
5. Check the rod. It will have a small gap when done the right way.



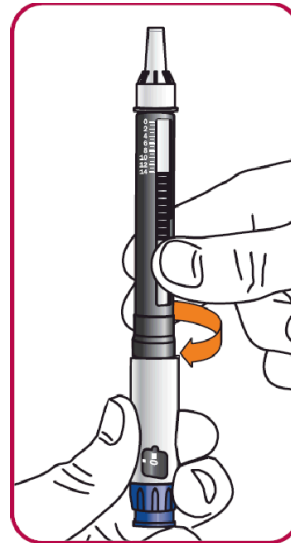
6. Unscrew the cartridge from the mixing device in a counterclockwise direction and put the mixing device down.



7. Attach the cartridge to the pen. Pick up the pen base and hold it with the rod pointed upright.

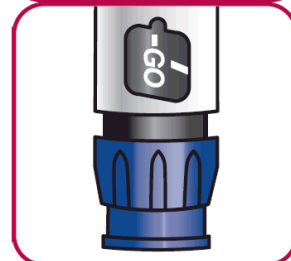


8. With the needle cap pointing up, screw the cartridge onto the pen in a clockwise direction until there is no space between the cartridge and the pen.

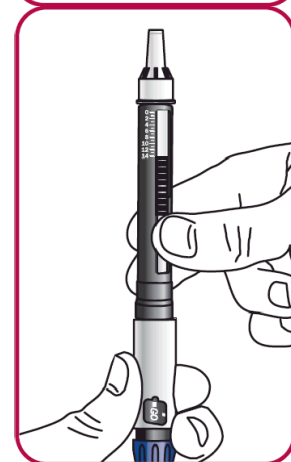


9. **Priming your Natpar pen.**

Turn the dosage knob in a clockwise direction until “GO” lines up with the notch in the dose window.

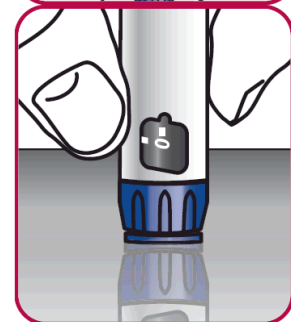


10. Hold the pen with the needle cap pointing up.



11. Press the injection button on a flat surface, such as a table top, until the “0” lines up with the notch in the dose window.

- It is normal for **1** or **2** drops of liquid to appear on the needle during this step.
- **Do not** remove the medicine cartridge from the pen until the “**Discard on**” date or the cartridge is empty.
- Prime your pen only **1** time for each new cartridge.



Giving your daily dose

NOTE: If you have just finished mixing your medicine and preparing your pen and the pen needle is on, go straight to “Before injecting your daily dose” (step 6 in this section) for instructions on how to inject using your Natpar pen.

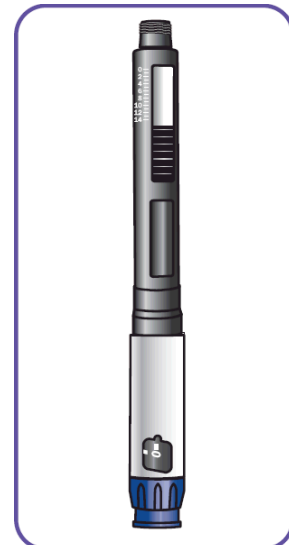
If you need help at any time, ask your doctor or nurse.

1. Wash and dry your hands.
2. Gather your supplies, including:
 - Your Natpar pen from the refrigerator
 - New disposable pen needle
 - Puncture resistant sharps container
 - Alcohol swab

Note: You should store your mixed cartridge within the pen in the refrigerator at all times, except when preparing and injecting your medicine.

3. **Check the cartridge.**

Remove the pen cap from your Natpar pen. The mixed cartridge should be inside.



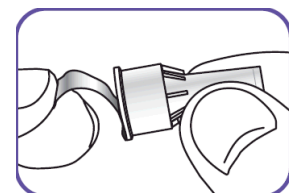
4. Before attaching a new needle to your pen, check:
 - If the solution is clear, **colourless** and free from visible particles. It is normal to see small bubbles.
If the liquid is not clear, colourless or free from visible particles, **do not use this medicine. Contact your doctor, pharmacist or nurse.**

You will have to prepare a new Natpar cartridge if:

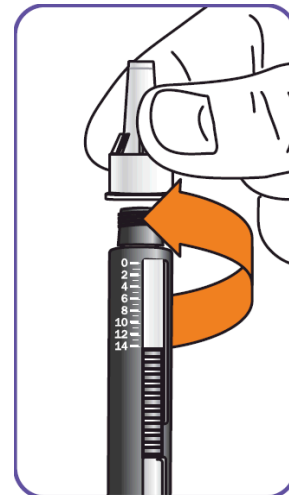
- There are no remaining doses in the pen (dose counter at “0”)
or
- The “**Discard on**” date has been reached (see medicine tracker).

5. Attaching a new needle.

- Remove the paper tab from the needle cap.
- Firmly hold the Natpar pen upright.
- While keeping the needle cap straight, screw it firmly onto the cartridge in a clockwise direction (the wider edge of the needle cap must touch the ‘shoulder’ of the



- cartridge).
- Leave the needle cap on.



6. **Before injecting your daily dose.**

- Do NOT use a cartridge that has been frozen.
- Discard all mixed cartridges if the “**Discard on**” date has been reached (see medicine tracker).

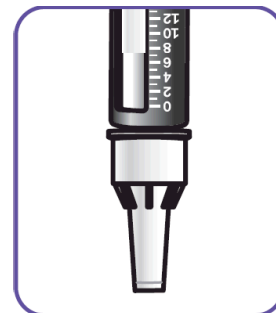
7. Wipe the injection area of your thigh with an alcohol swab.
Inject into an alternate thigh each day.



Make sure the needle cap is pointing downward at all times during step 8 to step 17.

8. Hold the Natpar pen **with the needle pointing straight down.**

- **Keep the needle pointing down until the injection is complete.**



9. Hold the pen so you can see the dose window.



10. Turn the dosage knob until “GO” lines up with the notch in the window. **Do not** turn the dosage knob past “GO.”

- **If the dosage knob is hard to turn**, you may not have enough liquid left. Check the **dose indicator** on the cartridge to see if there are any doses left or check the “**Discard on**” date on the **medicine cartridge tracker** to see if it has been more than **14** days.



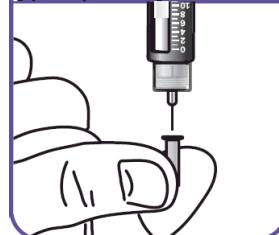
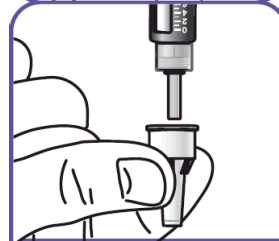
11. Gently tap the cartridge **3 to 5** times. This moves any air bubbles away from the needle.



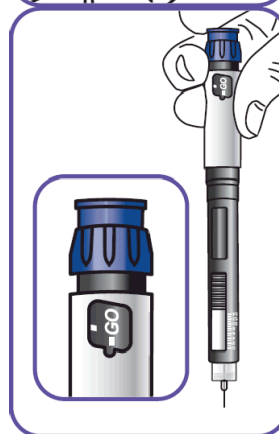
12. **Prepare the pen needle for giving the injection.**

Without unscrewing,

- Pull the needle cap straight off and set it aside.
- Then pull off the needle guard and discard it.



13. Hold the pen so you can see “GO” in the dose window with the pen needle pointing down.



14. Read steps **15**, **16**, and **17** carefully **before** you inject the medicine.

15. Insert the needle fully into your thigh (you can pinch a fold of the skin if told by your doctor or nurse). Make sure you can see “GO” in the window.



16. Press the injection button until the “0” lines up with the notch in the dose window. You should see and feel the dosage knob turn back to “0.” **Slowly count to 10.**



Important note about injecting:

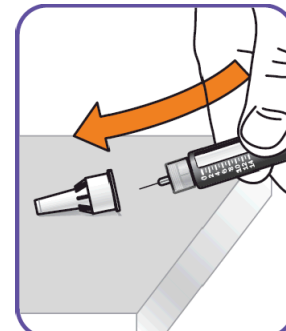
To avoid under-dosing, you will need to keep the needle in the skin for 10 seconds AFTER pressing the injection button.



17. Pull the needle straight out of your thigh.
- It is normal to see 1 or 2 drops of liquid appear on the needle during this step.
 - If you do not think you received your full dose, do not take another dose. Call your doctor. You may need to take calcium and vitamin D.

18. Carefully recap the exposed needle with the large needle cap by using a scooping technique.

- Make sure that the needle is pressed all the way into the cap.



19. Unscrew the needle cap (with the pen needle inside) in a counterclockwise direction while holding the cartridge.

- Do not share your pen or pen needles with anyone else. You may give an infection to them or get an infection from them.



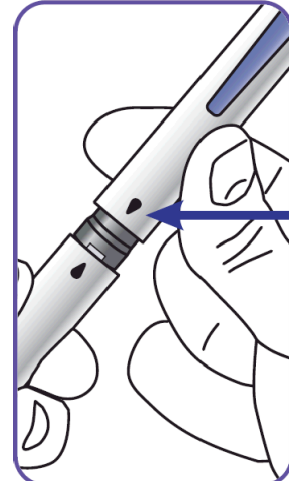
20. Discard the used needle into a puncture resistant container.

Ask your doctor, pharmacist or nurse how to properly dispose of a full puncture resistant container.



21. Put the cap back on your pen.

- A cartridge must be attached to the pen before you can put the pen cap on.
- Line up the pocket clip of the tab on the pen.
- Press the cap and pen together until you hear it click.



22. Place the Natpar pen in the refrigerator.

How to store your medicine

The Natpar cartridges and any pen that contains a mixed cartridge should always be stored in the refrigerator (2°C – 8°C).

- Do **NOT** freeze your cartridge.
- o **NOT** use a cartridge that has been frozen.
- d all mixed cartridges older than 14 days.