

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) 1986

This medicine is to be supplied by physician's prescription only

**Plegridy 63 mcg
Plegridy 94 mcg
Plegridy 125 mcg
Solution in a Pre-filled Pen**

Composition:

Each pen of **Plegridy 63** contains Peginterferon beta-1a 63 µg

Each pen of **Plegridy 94** contains Peginterferon beta-1a 94 µg

Each pen of **Plegridy 125** contains Peginterferon beta-1a 125 µg

*Please refer to section 6 (Additional information) for the list of inactive ingredients.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains essential information about this medicine. If you have any further questions, refer to the physician or the pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar.

This medicine is intended for the treatment of adults aged 18 or over.

1. What is this medicine intended for?

Plegridy is intended for the treatment of symptoms of relapsing-remitting multiple sclerosis.

Therapeutic group: Interferons.

Multiple sclerosis (MS) is a chronic illness that affects the central nervous system (CNS), including the brain and spinal cord. In this illness the body's immune system damages the protective layer (myelin) that surrounds the nerves in the brain and spinal cord. This disrupts the messages between the brain and other parts of the body, causing the symptoms of MS. In relapsing-remitting MS there are periods when the disease is not active (remission) in between flare-ups of symptoms (relapses). The disease can be manifested in various forms in different patients. The symptoms of multiple sclerosis include:

- Feeling off-balance or light headed, walking problems, stiffness and muscle spasms, tiredness, numbness in the face, arms or legs
- Acute or chronic pain, bladder and bowel problems, sexual problems and problems with vision
- Difficulty thinking and concentrating, depression.

Plegridy seems to prevent the immune system from damaging the brain and spinal cord. Its action helps to reduce the number of relapses and slow down the disabling effects of MS. Treatment with **Plegridy** can help to prevent your illness from getting worse, although it will not cure MS.

2. Before using this medicine:

Do not use this medicine if:

- You are sensitive (allergic) to Interferon-beta 1a or Peginterferon beta 1a or to any of the other ingredients that this medicine contains (see section 6)
- If you have severe depression or think about committing suicide.

Special warnings regarding the use of this medicine:

Before using Plegridy, tell your physician if:

- You suffer or have suffered in the past from depression or problems affecting your mood.
- You suffer or have suffered in the past from thoughts about committing suicide.
- You suffer from serious liver or kidney problems.
- You suffer from irritation at an injection site, which can lead to skin and tissue damage (injection site necrosis). Follow the injection instructions which appear at the end of this leaflet. This is to reduce the risk of injection site reactions.
- You suffer from epilepsy or other seizure disorders, not controlled by medicine.
- You suffer from heart problems, which can cause symptoms such as chest pain, particularly after any activity (angina); swollen ankles, shortness of breath (congestive heart failure); or an irregular heartbeat (arrhythmia).
- You suffer from thyroid problems.
- You suffer from a low number of white blood cells or platelets (which can cause an increased risk of infection, or bleeding).

Inform your doctor if one or more of these conditions applies to you. They may get worse while using **Plegridy**.

Additional warnings:

You will need blood tests – blood count, blood chemistry and your levels of liver enzymes. These tests should be performed before you start using **Plegridy**, regularly after treatment with **Plegridy** has been initiated and then periodically during treatment with **Plegridy**, even if you have no particular symptoms. These blood tests will be in addition to the tests which are normally done to monitor your MS.

The functioning of your thyroid gland should be checked regularly or whenever thought necessary by your physician.

Blood clots in the small blood vessels may occur during your treatment. These blood clots could affect your kidney function. This might happen several weeks to several years after starting **Plegridy**. Your physician will check your blood pressure, blood (platelet count) and the function of your kidneys.

If you accidentally prick yourself or someone else with the needle of **Plegridy**, the area affected should be washed immediately with soap and water and a physician should be contacted as soon as possible.

If you are about to undergo a blood test, you should notify the physician of your treatment with **Plegridy**. **Plegridy** may affect the blood test results.

Using in children and adolescents:

Plegridy is not to be used in children and adolescents below 18 years old. The safety and effectiveness of **Plegridy** in this age group are not known.

Tests and follow-up:

During treatment, you may be asked to perform blood tests - blood chemistry including liver function, complete and differential white blood cell count, thyroid function, and renal function.

Drug interaction

If you are taking or have recently taken other medicines, including nonprescription medications and nutritional supplements, inform your physician or pharmacist. In particular if you are taking:

- Other medicines that are broken down in the body by proteins called “cytochrome P450”, such as certain medicines used for epilepsy or depression.
- Medicines for the treatment of epilepsy or depression.

Notify the healthcare professionals of taking **Plegridy** if additional medicines are prescribed for you or if you have a blood test Plegridy may affect the other medicines or the test results.

Pregnancy, breastfeeding and fertility:

- If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist before talking this medicine.
- No harmful effects on the breastfed newborn/infant are anticipated. **Plegridy** can be used during breast-feeding.

Driving and using machines:

Plegridy has no or negligible influence on the ability to drive and use machines

Important information of part of the medication ingredients:

This medicine contains less than 1 mmol sodium (23 mg), that is to say it is essentially “sodium-free”.

3. How should you use the medicine?

Always use according to the physician’s instructions.

You should check with the physician or the pharmacist if you are unsure about your dose or about how to take this medicine.

The dosage and treatment will be determined only by the physician. You should start with the initial dose and then switch to maintenance dose. **The usual dose** for adults over 18 years is:

Maintenance dose

One injection of Plegridy 125 micrograms every 14 days (every two weeks). Try to use **Plegridy** at the same time on the same day of the week, every time you inject.

Starting Plegridy

If you are new to **Plegridy**, your doctor may advise you to gradually increase your dose so that you can adjust to the effects of **Plegridy** before taking the full dose. You will be provided with an Initiation Pack containing your first 2 injections: one orange pen with Plegridy 63 micrograms (for day 0) and one blue pen with Plegridy 94 micrograms (for day 14).

After that you will be provided with a maintenance pack containing grey pens with **Plegridy** 125 micrograms (for day 28 and then every two weeks).

Read the instructions in section 6 “*Additional information – Instructions for injecting Plegridy pre-filled pen*” at the end of this leaflet before you start using **Plegridy**.

Use the record table printed on the inside of the lid of the Initiation Pack to keep a track of your injection dates.

Do not exceed the recommended dose.

Injecting yourself – Plegridy is to be injected under the skin (*subcutaneous injection*). Alternate the sites you use for injections. Do not use the same injection site for consecutive injections. You can inject **Plegridy** yourself without the help of your doctor, if you have been trained how to do so. The instructions for self injection are provided at the end of this leaflet (see section 6). If you have trouble handling the pen, ask your doctor who may be able to help.

How long to use Plegridy

Your doctor will tell you how long you need to keep using **Plegridy**. It is important to continue using **Plegridy** regularly. Do not make changes unless your doctor tells you.

If you use more Plegridy than you should – You must only inject **Plegridy** once every 2 weeks. If you have used more than one injection of **Plegridy** in a 7-day period, **contact your doctor or pharmacist straight away**.

If you forget to use Plegridy – You need to inject **Plegridy** once every 2 weeks. This regular schedule helps to deliver the treatment as evenly as possible.

If you do miss your usual day, inject as soon as you can and carry on as usual.

However, do not inject more than once in a 7-day period. Do not use two injections to make up for a missed injection.

Continue with the treatment as recommended by the physician.

Even if there is an improvement in your health, do not stop treatment with this medicine without consulting the physician or the pharmacist

Do not take medicines in the dark! Check the label and the dose each time you take the medicine. Wear glasses if you need them.

If you have any further questions regarding the use of this medicine, consult the physician or the pharmacist.

4. Side effects

As with any medicine, the use of **Plegridy** may cause side effects in some patients. Do not be alarmed by reading the list of side effects. You may not experience any of them.

Severe side effects

Refer to your physician if you suffer from

- **Liver problems (common side effect - may affect up to 1 in 10 people)**

If you get any of these symptoms:

- Yellowing of your skin or the whites of your eyes
- Itching all over the body
- Feeling sick, being sick (*nausea and vomiting*)
- Easy bruising of the skin

They may be signs of a possible liver problem.

- **Depression (common side effect – may affect up to 1 in 10 people)**

If you:

- Feel unusually sad, anxious or worthless
- Have thoughts about suicide

- **Serious allergic reaction (uncommon side effect - may affect up to 1 in 100 people)**

If you get any of these symptoms:

- Difficulty breathing
- Swelling around the face (lips, tongue or throat)
- Skin rashes or redness

- **Seizures (uncommon side effect - may affect up to 1 in 100 people)**

- **Injection site damage (rare side effect - may affect up to 1 in 1,000 people)**

If you suffer from:

- Any break in the skin together with swelling, inflammation or fluid leaking around the injection site

- **Kidney problems including scarring that may reduce your kidney function (rare side effect - may affect up to 1 in 1,000 people)**

If you suffer from:

- Foamy urine
- Fatigue
- Swelling, particularly in the ankles and eyelids, and weight gain.

They may be signs of a possible kidney problem.

- **Blood problems (rare side effect - may affect up to 1 in 1,000 people)**

Blood clots may form in the small blood vessels that can affect your kidneys. Symptoms may include increased bruising, bleeding, fever, extreme weakness, headache, dizziness. Your physician may find changes in your blood tests and the function of your kidneys.

Additional side effects:

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

- Flu-like symptoms. These symptoms are not really flu (see below). You can't pass it on to anyone else.
- Headache
- Muscle pain (*myalgia*)
- Pain in your joints, arms, legs or neck (*arthralgia*)
- Chills
- Fever
- Feeling weak or tired (*asthenia*)
- Redness, itching or pain around the place you have injected

These symptoms are not really flu. They are more common when you first start using **Plegridy**. Later on they will gradually get less. Ways to cope with flu-like symptoms:

1. Consider the timing of your injection. The start and end of flu-like symptoms are different for every patient. On average, flu-like symptoms begin approximately 10 hours after injection and last between 12 and 24 hours.
2. Take paracetamol or ibuprofen half an hour before your **Plegridy** injection and continue to take paracetamol or ibuprofen for the duration of your flu-like symptoms. Speak to your physician or pharmacist about the right dose.
3. If you have a fever, drink plenty of water to avoid dehydration.

Common side effects (may affect 1 in 10 people) –

- Feeling or being sick (*nausea or vomiting*),
- Hair loss (alopecia),
- Itchy skin (*pruritus*),
- Increase in body temperature,
- Warmth/ bruising/ rash/ swelling/ colour change or inflammation around the place you have injected,
- Changes in your blood which might cause tiredness or reduced ability to fight infection
- Increases in liver enzymes in the blood, (will show up in blood tests)

Uncommon side effects (may affect 1 in 100 people) –

- Hives
- Changes in your blood which might cause unexplained bruising or bleeding.

Side effects with unknown frequency (side effects for which the frequency cannot be estimated from the available data) –

- Pulmonary arterial hypertension.
A disease of severe narrowing of the blood vessels in the lungs resulting in high blood pressure in the blood vessels that carry blood from the heart to the lungs. Pulmonary arterial hypertension has been seen at various time points during treatment, including several years after starting treatment with interferon beta-products.

If a side effect occurs, if any side effect gets worse, or if you suffer from a side effect not mentioned in the leaflet, you should consult the physician.

Side effects can be reported to the Ministry of Health (MoH) by clicking on the "Report on side effects due to medication therapy" link on the MoH home page (www.health.gov.il) which refers to the online form for side effects reporting, or by entering the link: <https://sideeffects.health.gov.il/>

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without explicit instructions from the physician.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- Storage conditions: store under refrigeration (2-8°C: this temperature range is typical of most home refrigerators).
Do not freeze. Throw away any Plegridy that is accidentally frozen.
Store in the original package in order to protect from light. You should open a new package only if you need a new pen.
Can be stored up to 30 days at the temperature of 25°C; do not use the medicine beyond this period
Take the medicine out of the refrigerator about 30 minutes prior to the injection.

Do not use Plegridy if you notice any of the following:

- The solution is non-transparent, cloudy or you can see particles floating in it.
- The pen is broken.

Do not discard the medicine to the sewers. Consult the pharmacist about how to dispose of the medicine.

6. Additional information:

- In addition to the active ingredient the medicine also contains:
Sodium acetate trihydrate, glacial acetic acid, arginine hydrochloride, polysorbate 20, water for injection.
- What does the medicine look like and what are the contents of the package:
Plegridy 125 as pen – a box containing either two or six pre-filled pens (grey). Each dose is packed separately and contains a pen, a needle and a pen cover. The pre-filled pen contains 0.5 ml of clear solution.
Plegridy 63, 94 as pen – a box containing one pen (orange) of **Plegridy 63 mcg** and one pen (blue) of **Plegridy 94 mcg**.

Not all packs may be marketed.

- Manufacturer and address: Biogen Netherlands B.V, The Netherlands.
- Registration holder and address: Medison Pharma Ltd., 10 Hashiloach St., P.O.B 7090 Petach Tikva
- For patient support program dial *5274
- This leaflet was reviewed and approved by the Ministry of Health in December 2015 and revised in accordance with Ministry of Health guidelines in December 2019.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Plegridy 63: 155-02-34287
Plegridy 94: 155-03-34291
Plegridy 125: 155-04-34292

How to Inject Plegridy?

Caution! Do not remove the cap until you are ready to inject.

Read the instructions for use before you start using **Plegridy** and each time you get a refill of your prescription. There may be new information. This information does not take the place of talking to your doctor about your medical condition or your treatment.

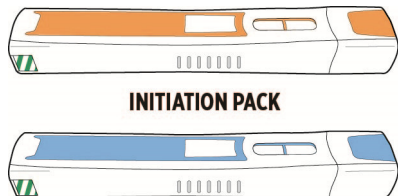

You can inject the medicine yourself only if you have been adequately trained to use the injection technique. The explanations provided below are instructions; if you do not feel confident, check with the physician or the pharmacist.

Note:

- **Before you use the pen for the first time**, your doctor or nurse should show you or your carer how to prepare and inject the pen.
- **Plegridy** is for use under the skin only (subcutaneous).
- Each pen can be used once only.
- **Do not share** the pen with anyone else to avoid giving an infection to them or getting an infection from them.
- **Do not use more than 1** pen every 14 days (every 2 weeks).
- **Do not** use the pen if it has been **dropped or is visibly damaged**.
- **Change the injection site every week to reduce the risk of irritation of the skin or the muscle.**
- **Avoid injecting into injured, irritated, infected or scarred skin areas or into an open wound area**
- **Examine the injection area about 2 hours following injection. If you have a skin reaction which does not resolve within several days, contact the physician or the nurse.**

Dosage schedule

The Initiation Pack contains your first two injections to gradually adjust your dose. Choose the correct pen from a pack.

When	Which dose	Which pack
Day 0 (63 micrograms)	First injection: 63 micrograms, choose orange pen	 <p>INITIATION PACK</p>
Day 14 (94 micrograms)	Second injection: 94 micrograms, choose blue pen	
Day 28 and then every two weeks after that (125 micrograms)	Full dose injection: 125 micrograms, choose grey pen	 <p>125 MICROGRAM PACK</p>

Do not use more than one pen per 14-day period (every 2 weeks).

Supplies needed for your Plegridy Pen injection:

- 1 Plegridy Pen (see Figure A)

Before use – Parts of Plegridy Pen (Figure A)

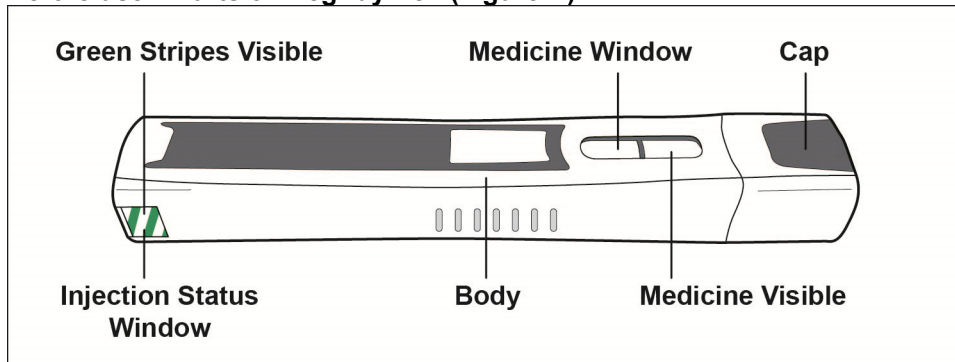


Figure A

Caution! Do not remove the cap until you are ready to inject. If you remove the cap, do not re-cap the pen. Re-capping could cause the pen to lock.

Additional supplies which are not included in the pack (see Figure B):



Figure B

Preparing for your injection:

Step 1: Remove your pen from the fridge

- a. Remove your Plegridy pack from the fridge and select the appropriate pen (dosage) from the pack.
- b. Close the pack and put back in the fridge after removing one pen.
- c. **Let the pen warm to room temperature for at least 30 minutes.**
*Do not use external heat sources, such as hot water, to warm your pen.

Step 2: Collect your supplies and wash your hands

- a. Find a well-lit, clean, flat surface to work on like a table. Collect all the supplies you will need to give yourself, or receive, an injection.
- b. Wash your hands thoroughly with soap and water.

Step 3: Check your Plegridy pen (see Figure C)

- a. Check the injection status window. You should see green stripes.
 - b. Check the expiry date.
 - c. Check the medicine window and make sure the Plegridy medicine is clear and colourless.
- Do not** use the pen if:
- **You do not see the green stripes** in the injection status window.
 - **It is expired.**
 - **The liquid is coloured, cloudy or contains floating particles.**

Note: You might see air bubbles in the medicine window. This is normal and will not affect your dose.

***Do not use** the pen if it has been **dropped or is visibly damaged.**

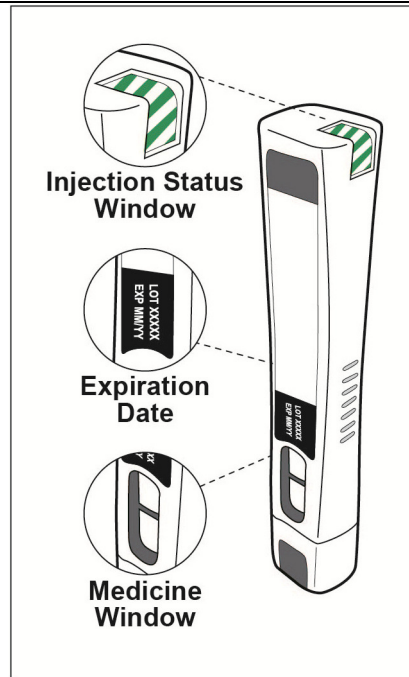


Figure C

Step 4: Choose and clean your injection site

- a. Choose an injection site in your thigh, abdomen, or the back of your upper arm (see highlighted areas in Figure D).
 - If some areas are too difficult for you to reach, ask a carer who has been trained to help you.
 - **Do not** inject into an area of your body where **the skin is irritated, red, bruised, tattooed, infected, or scarred.**
 - **Do not** inject directly **into your belly button.**
- b. Wipe your skin with an alcohol wipe.
 - **Note: Do not touch or blow** on this area again before giving your injection.
- c. Let your injection site dry on its own before injecting your dose.

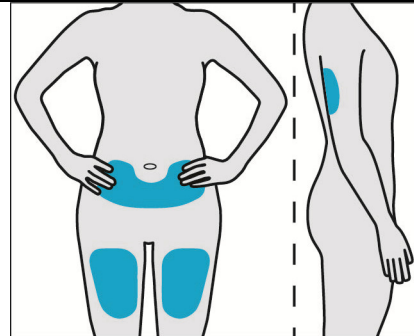


Figure D

Giving your injection

Step 5: Remove the Plegridy pen cap

- a. Pull the pen cap straight off and set it aside (see Figure E). Your pen is now ready to inject.
- **Warning! Do not** touch, clean, or manipulate the needle cover. You could get a needle injury or the pen may lock.
 - **Caution! Do not** re-cap your pen. This could lock the pen

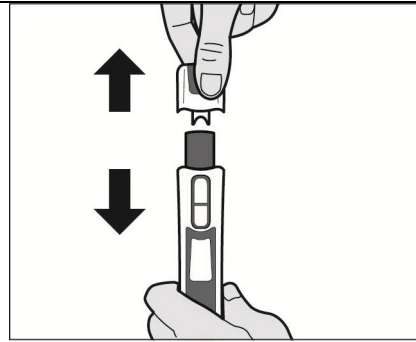


Figure E

Step 6: Give the injection

- a. Hold the pen over your injection site. Make sure you can see the green stripes in the injection status window (see Figure F).
- You should hold the pen over your injection site at a 90° angle.
 - **Warning! Do not** rest the pen on the injection site until you are ready to inject. This may cause the pen to accidentally lock.

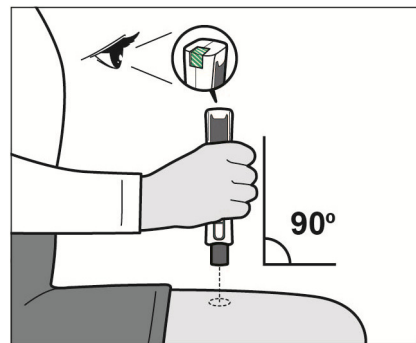


Figure F

- b. Firmly press and hold down the pen on your injection site. You will hear the clicking sounds start. This tells you that the injection is happening (see Figure G).

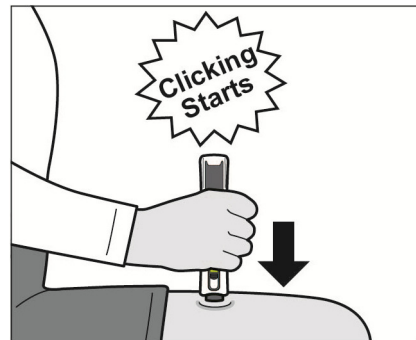


Figure G

- c. Continue to hold the pen firmly down on your injection site until the clicking sounds have stopped (see Figure H).

- **Do not** lift your pen off your injection site until the clicking sounds stop and you see green ticks in the injection status window.
- **Warning! If you do not hear clicking sounds or you do not see green ticks** in the injection status window after attempting to inject, the pen may have locked and you may not have received your injection. You should then **contact your doctor**.

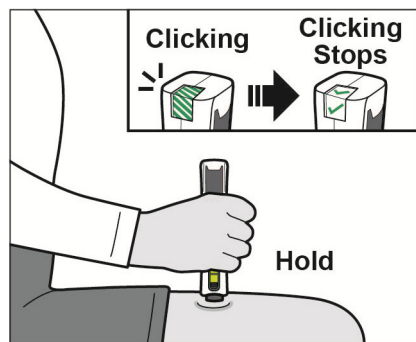


Figure H

Step 7: Remove the Plegridy pen from your injection site

- a. After the clicking sound has stopped, lift the pen from your injection site. The needle cover will extend to cover the needle and will lock (see Figure I).
- If you see blood at your injection site, wipe it off with the gauze pad and apply an adhesive bandage or plaster.

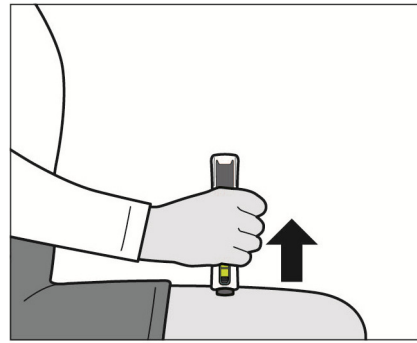


Figure I

Step 8: Check to make sure you received your full dose of Plegridy (see Figure J)

- a. Check the injection status window. You should see green ticks.
- b. Check the medicine window. You should see a yellow plunger.

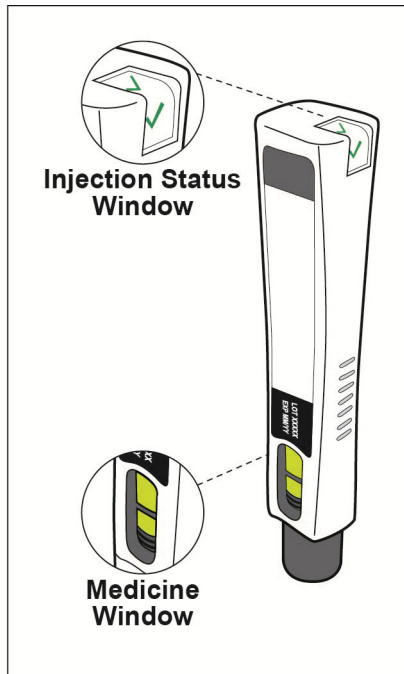


Figure J

After the injection

After Use – Parts of your Plegridy pen (see Figure K):

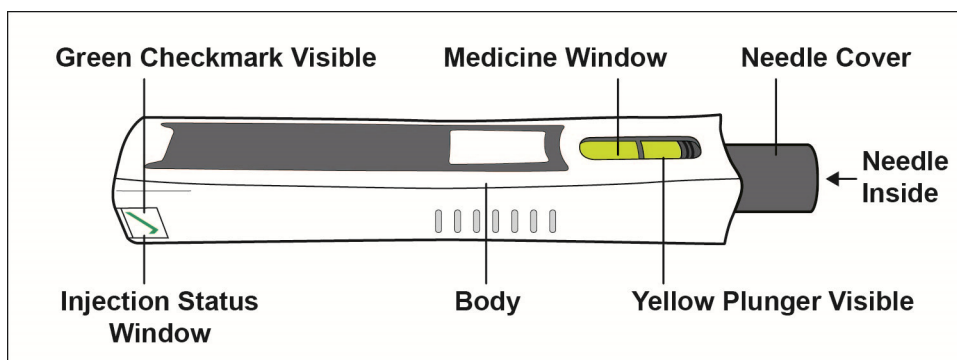


Figure K

Note: After the pen has been removed from the injection site, the needle cover will lock to protect against needle injury. **Do not re-cap the pen.**

Step 9: Dispose of used Plegridy pen

- Check with your doctor, pharmacist or nurse about the right way to throw away the used pen.
- **Do not re-cap the pen.**

Step 10: Care for your injection site

If needed, apply a gauze pad or adhesive bandage or plaster to the injection site.

Step 11: Check injection site

After 2 hours, check the injection site for redness, swelling, or tenderness.

If you have a skin reaction and it does not clear up in a few days, contact your doctor.

Record date and location

- Record the date and location of each injection.
- For the Initiation Pack injections, you can use the record table printed on the inside of the lid of the Initiation Pack.

General warnings

- Do not reuse your **Plegridy** pen.
- Do not share your **Plegridy** pen.
- **Keep Plegridy pen and all medicines out of reach of children.**

PLEGRIDY-PIL-08/23-V1